

Prescription for costly health care

Program by some insurers to encourage patients to cut pills in half has critics -- especially drug firms that would lose money

Victoria Colliver, Chronicle Staff Writer

Tuesday, May 30, 2006

Some of the country's largest health insurers are encouraging patients to save money by splitting their pills in half.

By purchasing a higher dose and slicing the pills into two parts, patients also cut their co-payments in half. But this practice, long used by uninsured people and Medicare patients before the program had a drug benefit, is as controversial as it is low tech.

Pill-splitting critics warn that some patients may not cut their tablets accurately, leading to potential under-doses or overdoses of medication. They say people with cognitive impairments, poor vision or arthritis may be especially prone to errors.

But, with such companies as UnitedHealth Group, the nation's second-largest health insurer, promoting a Half Tablet Program, the practice has received a powerful endorsement.

"As consumers are having to become better educated and are picking up a bigger share of their costs, this may be in their best interest," said UnitedHealth spokesman Tyler Mason.

UnitedHealth is taking advantage of the fact that drug manufacturers typically charge the same amount for, say, 10-milligram and 20-milligram doses of the same medication.

Patients who need a 10-milligram dose can purchase a 30-day supply of 20-milligram tablets, cut the pills in half and pay just one co-payment for a two-month supply. That means members who are charged \$50 in co-payments for brand-name drugs can save \$300 a year, according to UnitedHealth.

After testing the concept in Wisconsin early last year, UnitedHealth has taken it nationwide. The insurer is only offering the program on a voluntary basis for 16 drugs that it deems safe to split. The drugs treat such conditions as depression, hypertension and high cholesterol.

UnitedHealth sent letters to patients taking those drugs and has filled requests for 28,000 pill-splitting devices.

The Veterans Affairs Department, which operates the nation's largest health system, saved \$46.5 million in 2003 by having eligible patients halve a popular cholesterol-lowering drug sold under the brand-name Zocor. Department researchers found no difference in cholesterol levels or liver functions between those who split pills and those who took the equivalent doses in the form of single pills in a 1999 study of 3,787 patients in Florida, Puerto Rico and Georgia.

Drug manufacturers, which stand to lose a lot of money if the practice takes off, are among the biggest foes of pill splitting.

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"Health care professionals have noted that this practice can be dangerous, unsafe and should not be encouraged," said Ken Johnson, senior vice president of the Pharmaceutical Research and Manufacturers of America, the drug industry's main trade group.

Kaiser Permanente had been an early proponent of tablet splitting. But in 2000, a group of former and current members, along with a Kaiser physician, filed suit over the issue, claiming the HMO giant was endangering patients to save money.

After Kaiser won the case on a summary judgment, the state Supreme Court refused to review the decision. Kaiser continues to encourage its members to split tablets when minor dosage variations are acceptable.

Fresno emergency physician Charles Phillips, the doctor involved in the Kaiser lawsuit, says pill splitting is never safe. He said a 15-year-old study showed a 20 percent variance in weight of split tablets. While studies have not shown patient harm, no study has confirmed the practice is safe, he said.

Although patients may save in co-payments, insurers are the big winners, Phillips said. "Usually this is money siphoned off into the (insurer's) profits," he said.

The California Medical Association does not endorse the practice.

"There are obviously going to be some people who split pills inaccurately, get confused and get a non-therapeutic dose or suffer adverse consequences," said Dr. Jack Lewin, chief executive officer of the doctors' group. He suggested insurers lobby drugmakers to lower prices for reduced-dosage medications rather than encourage member to halve their tablets.

Consumer groups generally support pill splitting, as long as patients consult their physicians.

"Virtually nobody who has looked at this practice in the real world ... has ever found a problem with it at all," said Steve Findlay, health policy analyst for Consumers Union.

Findlay cautioned that tablet splitting is not right for everyone. "Insurers are entering this very delicately," he said. "Everyone just wants to be cautious here so they don't send a signal broadly to the public that this is something you should be doing willy-nilly."

In addition to their physicians, patients also need to inform their insurers they are splitting their tablets, said Michael Negrete, vice president of clinical programs for the California Pharmacists Association.

Pharmacists may encounter billing or patient compliance problems if they bill an insurer for a 30-day prescription for a customer who intends that medication to last for 60 days, Negrete said. Billing problems are not a concern when the insurer sponsors a tablet-halving program.

Negrete said pill splitting can be safe under certain circumstances with specific medications. However, he said drugmakers may eventually stop selling higher dosages at the same price as the lower-strength medicine.

"One man's savings is another man's lost revenue," he said. "If this becomes a more common occurrence with

other health plans, I would expect a situation in which the manufacturers change their pricing strategies to take this incentive away."

Pill-splitting tips

- Always consult your physician before splitting any medication. Time-release formulations, plastic capsules and pills with special coatings should not be split.
- Use a pill-splitting device rather than a knife or a razor. Pill splitters are sold in drugstores.
- Only split tablets in half. Pills can crumble when split more than once.
- To ensure the most accurate dosage, split tablets one at a time and take the segments on consecutive days.

Source: Chronicle research

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<http://sfgate.com/cgi-bin/article.cgi?f=/c/a/2006/05/30/BUGF8J3D9H1.DTL>

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ISMP Medication SafetyAlert!

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SafetyBriefs



ICAHO changes standard.

A change in the Joint Commission standards, specifically the Element of Performance #2 for standard MM.4.50, will affect many organizations that do not provide round-the-clock pharmacy services. Previously, the Joint Commission allowed nursing access to a limited section of the pharmacy to retrieve medications after hours, when allowed by law and regulation, if other requirements in the Elements of Performance were met. After July 1, 2006, access to any part of the pharmacy by non-pharmacist personnel after hours is not allowed, even if permitted by law and regulation. All after-hours medications must be stored outside of the pharmacy (e.g., in a night cabinet, automated dispensing cabinet). If a needed drug is not available in that supply, an on-call pharmacist must come in to retrieve it or the medication must be obtained from an outside pharmacy that is open. This change was first announced in the February 2006 issue of *Perspectives* and was released in final form in the recent update to the *Comprehensive Accreditation Manual for Hospitals* that was sent to all accredited hospitals and Manual owners. Patients are at risk when non-pharmacists have complete access to a pharmacy after hours. With current technology, planning, and cooperation from medical and nursing staff, night access to the pharmacy can be eliminated, even in rural hospitals.



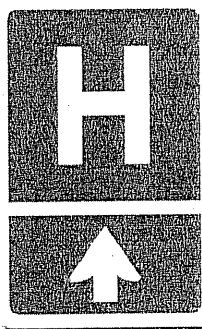
Read-back works. Physicians at

Cincinnati Children's Hospital Medical Center recently studied error rates with and without the use of *read-back* of orders given verbally and then entered into the computerized prescriber order entry system. The Joint Commission National Patient Safety Goal 2A requires such a *read-back* process for both oral orders and oral critical test results. In the Cincinnati facility, the attending physician or chief resident typically communicates orders verbally during rounds and a resident physician then enters them into the computer system at a

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Tablet splitting: Do it only if you "half" to, and then do it safely

PROBLEM: Most oral medications are available commercially in the dosage strengths most commonly prescribed for patients. Occasionally, the patient's exact dose is not available commercially, so more than one tablet or just part of a tablet may be needed. While using more than one tablet for a single dose is customary, tablet splitting has become more commonplace in the past 5 years for several reasons:



■ Different tablet strengths often cost about the same. Patients who cannot afford their medications have received a higher strength tablet with directions to take ½ tablet (or even ¼ tablet) per dose.¹

■ Some health insurers have denied payment of prescriptions for the lower strength of certain drugs, thus requiring patients to receive the higher strength tablet and split it in half for each dose.¹

■ Some healthcare organizations have not purchased all commercially available strengths of oral medications. Thus, some of the drugs may require tablet splitting for patient-specific doses in the inpatient setting.

■ Patients may not be able to swallow whole tablets.²

A recent article in the Veterans Administration (VA) *Topics in Patient Safety* newsletter,² and a 2002 article on the American Society of Consultant Pharmacists website, *Tablet Splitting for Cost Containment*, authored by Thomas Clark,¹ offer several pitfalls with splitting tablets that clearly suggest it is not the safest option if the patient-specific dose is available commercially.

Patient factors. First, it is easy for patients to become confused about the correct dose. One woman learned this when she was admitted to the hospital with unstable angina and hypertension. Her physician found that she had been taking the wrong dose of lisinopril. She was supposed to be taking 5 mg BID, but the prescription label said there were 10 mg tablets in the

bottle. When the physician looked inside, he saw both pink and peach tablets, some of which were split in half. Initially, the patient had been taking a 20 mg tablet BID. When her physician lowered the dose to 10 mg BID, she had the new prescription filled. The patient then cut the leftover 20 mg tablets in half and put them in the same bottle that held the 10 mg tablets. Later, her physician lowered the dose to 5 mg BID. Instead of filling the new prescription for 5 mg tablets, she tried to find all the 10 mg tablets to split them in half, but some remained whole.

In this case, no one could be certain of the dose the patient had been taking before she was hospitalized. But a study by the VA showed that most people took *too much* medication because they forgot to split their tablets.² Between January 2001 and April 2005, the VA's National Center for Patient Safety database included 442 reports related to pill splitting. Of those, 38% were considered adverse events, mostly occurring in outpatient settings (65%). Two-thirds of the patients received more than the intended dose. Pharmacists caught these errors because the patients came in too soon to refill their prescriptions. A quarter of the medications were high-alert drugs. About 9% of patients were harmed by these mistakes; 2% required hospitalization. In more than half of the events, the involved doses were available commercially.

Clark identified a few additional risks with tablet splitting:¹

■ A pharmacist might misread a prescription written for 1/2 tablet as 1-2 tablets.

■ Patients may assume the tablets have already been split when they have not, or split them again when they have been split already (especially if the pharmacy inconsistently splits the tablets upon refill).

■ Patients may not have the visual acuity or manual dexterity needed to split the tablets.

■ Patients may get confused and split the

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SafetyBriefs continued

bedside terminal. In the first part of the study, the team on rounds accepted 70 consecutive oral orders and entered them into the computer. After rounds, they examined the orders and found a 9.1% error rate, mostly in drug dosages that would not have affected patient safety. However, in two instances, the resident ordered the wrong drug. In the second part of the study, before leaving a patient's room, the resident read back the order entered into the computer. The attending physician or chief resident then verified its accuracy. The researchers examined 75 orders and found that the error rate dropped from 9.1% to zero. The process added only seconds to each visit to a patient's room, so it did not slow down physician rounding. The data were presented last month at the Pediatric Academic Societies' annual meeting in San Francisco and will eventually be published (visit www.cincinnatichildrens.org/about/news/release/2006/5-verbal-order-errors.htm).

Special Announcements

Self-assessment data. Thanks to all who participated in the *2005 ISMP Medication Safety Self Assessment® for Antithrombotic Therapy in Hospitals*. Preliminary aggregate data are now available to those who anonymously submitted their findings to ISMP. Visit www.ismp.org/selfassessments/asa/Intro.asp and use the password provided during the data submission process to view the aggregate results. The self-assessment remains open to those who still want to participate. Results will be updated in real time as new participants join the study.

ISMP teleconference. Our next teleconference, *The Impact of Clinical Decision Support Systems: Alerts and Standardized Order Sets*, will be held on June 29 from 1:30-3:00 p.m. EDT. The quantity and quality of safety alerts generated by computerized prescriber order entry (CPOE) systems is often problematic. Our guest speaker, **Eric Pifer, MD**, Chief Medical Informatics Officer at the University of Pennsylvania, will discuss how to best use safety alerts and order sets to augment decision making when prescribing drugs. **Peter Kilbridge, MD**, Associate Chief Information Officer for Patient Safety and Clinical Effectiveness at Duke University will moderate and discuss the Leapfrog initiative for evaluating hospital CPOE systems. For more information, visit: www.ismp.org/educational/teleconferences.asp.

Tablet splitting continued

wrong medication, or get tired of splitting the tablets and stop taking it.

■ *To maximize cost savings, the patient may have been told to split the tablets in half, but the directions on the prescription may list "1 tablet" for each dose. These directions could mislead the patient or other health-care providers who use the prescription label as a source of information when gathering a patient's medication history.*

■ *Split tablets crumble more easily.*

Medication factors. Some medications or formulations are not suitable for splitting, including:

- Enteric-coated/extended-release tablets
- Very small tablets
- Asymmetrical tablets
- Capsules
- Teratogenic medications (e.g., bosenan).

Clark cites various studies that suggest that the accuracy of split tablets is questionable, even if the tablet is scored.¹ In one study, 94 volunteers were asked to split 10 tablets of hydrochlorothiazide 25 mg; 41% of the split tablets deviated by 10% of the correct weight, and 12% deviated by more than 20%. After the study, two-thirds of the volunteers said they would be willing to pay more for commercially available tablets in the correct strength. Other research cited by Clark corroborates the significant variation in tablet halves with rates of inaccuracy ranging from 5-72%.

SAFE PRACTICE RECOMMENDATIONS: Healthcare providers should make every effort to use commercially available oral tablets when available in both inpatient and outpatient settings. However, tablet splitting may still be necessary if the drug is not commercially available in the patient-specific dose, or if the patient's inability to afford the medication as an outpatient outweighs the risks involved with tablet splitting. Under these circumstances, consider the following suggestions from Clark, the VA, and ISMP:

Verify suitability. Before prescribing, dispensing, or administering half tablets, check drug references to ensure that it is safe. If unsure, contact the manufacturer.²

Select patients carefully. Establish criteria to screen patients before prescribing or dispensing half tablets to ensure they have the required level of understanding, ability, and motivation to split the tablets.^{1,2} Ensure that the patient understands the risks associated with tablet splitting. If the patient cannot be expected to split his or her own tablets, enlist the aid of a qualified family member. (Note: It may not be legal in some states for a pharmacist to split tablets if the dose is available commercially.¹)

Dispense split tablets for inpatients. For hospitalized patients, pharmacy staff should dispense exact doses by either splitting tablets and repackaging them or preparing an oral solution in a unit-dose oral syringe for each dose. Nurses should not be expected to split the tablets.

Keep it clean. Patients and healthcare providers who split tablets should wash their hands first. Healthcare providers should also wear gloves. If a tablet-splitting device is used, it should be washed afterwards to remove any powder or particles.

Prescribe by weight. Prescribers should order the medication strength and dose in "mg" when possible to avoid misreading an order for a "1/2" tablet as 1-2 tablets.

Counsel patients. Establish a system to ensure patient counseling when prescriptions for medications that require half tablets are picked up at community pharmacies, even if the pharmacist has split the tablets for the patient.²

Provide the right tools. If patients must split tablets at home, provide them with a tablet-splitting device to improve the accuracy.²

Provide discharge education. If patients are receiving half tablets while in the hospital, advise them regarding the dose they should take after discharge and whether this requires split or whole tablets.

References: 1) Clark TR. Tablet splitting for cost containment. August 2002. Available at: www.ascp.com/advocacy/briefing/tabletsplittingcontainment.cfm. 2) Sales MM, Cunningham FE. Tablet splitting. *Topics in Patient Safety (TIPS)*. 2006;6(3):1,4.

INSTITUTE FOR SAFE MEDICATION PRACTICES

Normal View

TABLET SPLITTING: DO IT ONLY IF YOU "HALF" TO, AND THEN DO IT SAFELY

From the May 18, 2006 issue

Problem: Most oral medications are available commercially in the dosage strengths most commonly prescribed for patients. Occasionally, the patient's exact dose is not available commercially, so more than one tablet or just part of a tablet may be needed. While using more than one tablet for a single dose is customary, tablet splitting has become more commonplace in the past 5 years for several reasons:

- Different tablet strengths often cost about the same. Patients who cannot afford their medications have received a higher strength tablet with directions to take $\frac{1}{2}$ tablet (or even $\frac{1}{4}$ tablet) per dose (1).
- Some health insurers have denied payment of prescriptions for the lower strength of certain drugs, thus requiring patients to receive the higher strength tablet and split it in half for each dose (1).
- Some healthcare organizations have not purchased all commercially available strengths of oral medications. Thus, some of the drugs may require tablet splitting for patient-specific doses in the inpatient setting.
- Patients may not be able to swallow whole tablets (2).

A recent article in the Veterans Administration (VA) Topics in Patient Safety newsletter (2) and a 2002 article on the American Society of Consultant Pharmacists website, Tablet Splitting for Cost Containment, authored by Thomas Clark (1), offer several pitfalls with splitting tablets that clearly suggest it is not the safest option if the patient-specific dose is available commercially.

Patient factors. First, it is easy for patients to become confused about the correct dose. One woman learned this when she was admitted to the hospital with unstable angina and hypertension. Her physician found that she had been taking the wrong dose of lisinopril. She was supposed to be taking 5 mg BID, but the prescription label said there were 10 mg tablets in the bottle. When the physician looked inside, he saw both pink and peach tablets, some of which were split in half. Initially, the patient had been taking a 20 mg tablet BID. When her physician lowered the dose to 10 mg BID, she had the new prescription filled. The patient then cut the leftover 20 mg tablets in half and put them in the same bottle that held the 10 mg tablets. Later, her physician lowered the dose to 5 mg BID. Instead of filling the new prescription for 5 mg tablets, she tried to find all the 10 mg tablets to split them in half, but some remained whole.

In this case, no one could be certain of the dose the patient had been taking before she was hospitalized. But a study by the VA showed that most people took too much medication because they forgot to split their tablets (2). Between January 2001 and April 2005, the VA's National Center for Patient Safety database included 442 reports related to pill splitting. Of those, 38% were considered adverse events, mostly occurring in outpatient settings (65%). Two-thirds of the patients received more than the intended dose. Pharmacists caught these errors because the patients came in too soon to refill their prescriptions. A quarter of the medications were high-alert drugs. About 9% of patients were harmed by these mistakes; 2% required hospitalization. In more than half of the events, the involved doses were available commercially.

Clark identified a few additional risks with tablet splitting (1):

- A pharmacist might misread a prescription written for $\frac{1}{2}$ tablet as 1-2 tablets.
- Patients may assume the tablets have already been split when they have not, or split them again when they have been split already (especially if the pharmacy inconsistently splits the tablets upon refill).
- Patients may not have the visual acuity or manual dexterity needed to split the tablets.
- Patients may get confused and split the wrong medication, or get tired of splitting the tablets and stop taking it.
- To maximize cost savings, the patient may have been told to split the tablets in half, but the directions on the prescription may list "1 tablet" for each dose. These directions could mislead the patient or other healthcare providers who use the prescription label as a source of information when gathering a patient's medication history.

- Split tablets crumble more easily.

Medication factors. Some medications or formulations are not suitable for splitting, including:

- Enteric-coated/extended-release tablets
- Very small tablets
- Asymmetrical tablets
- Capsules
- Teratogenic medications (e.g., bosentan).

Clark cites various studies that suggest that the accuracy of split tablets is questionable, even if the tablet is scored.¹ In one study, 94 volunteers were asked to split 10 tablets of hydrochlorothiazide 25 mg; 41% of the split tablets deviated by 10% of the correct weight, and 12% deviated by more than 20%. After the study, two-thirds of the volunteers said they would be willing to pay more for commercially available tablets in the correct strength. Other research cited by Clark corroborates the significant variation in tablet halves with rates of inaccuracy ranging from 5-72%.

Safe Practice Recommendations: Healthcare providers should make every effort to use commercially available oral tablets when available in both inpatient and outpatient settings. However, tablet splitting may still be necessary if the drug is not commercially available in the patient-specific dose, or if the patient's inability to afford the medication as an outpatient outweighs the risks involved with tablet splitting. Under these circumstances, consider the following suggestions from Clark, the VA, and ISMP:

Verify suitability. Before prescribing, dispensing, or administering half tablets, check drug references to ensure that it is safe. If unsure, contact the manufacturer.² Select patients carefully. Establish criteria to screen patients before prescribing or dispensing half tablets to ensure they have the required level of understanding, ability, and motivation to split the tablets (1,2). Ensure that the patient understands the risks associated with tablet splitting. If the patient cannot be expected to split his or her own tablets, enlist the aid of a qualified family member. (Note: It may not be legal in some states for a pharmacist to split tablets if the dose is available commercially [1]).

Dispense split tablets for inpatients. For hospitalized patients, pharmacy staff should dispense exact doses by either splitting tablets and repackaging them or preparing an oral solution in a unit-dose oral syringe for each dose. Nurses should not be expected to split the tablets.

Keep it clean. Patients and healthcare providers who split tablets should wash their hands first. Healthcare providers should also wear gloves. If a tablet-splitting device is used, it should be washed afterwards to remove any powder or particles.

Prescribe by weight. Prescribers should order the medication strength and dose in "mg" when possible to avoid misreading an order for a "1/2" tablet as 1-2 tablets.

Counsel patients. Establish a system to ensure patient counseling when prescriptions for medications that require half tablets are picked up at community pharmacies, even if the pharmacist has split the tablets for the patient (2).

Provide the right tools. If patients must split tablets at home, provide them with a tablet-splitting device to improve the accuracy (2).

Provide discharge education. If patients are receiving half tablets while in the hospital, advise them regarding the dose they should take after discharge and whether this requires split or whole tablets.

References: **1)** Clark TR. Tablet splitting for cost containment. August 2002. Available at: www.ascp.com/advocacy/briefing/tabletsplittingcontainment.cfm. **2)** Sales MM, Cunningham FE. Tablet splitting. Veterans Administration Topics in Patient Safety (TIPS). 2006;6(3):1,4.

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Preventing Errors with Tablet Splitting

FDA Patient Safety News: Show #54, August 2006

Splitting tablets is a common practice where tablets of a higher strength than the patient needs are broken in half, or even quarters, to provide the correct dose. This is often done to reduce costs, since the higher strength tablet sometimes costs about the same as the lower strength one. In some cases the hospital may not stock the lower strength of a particular medication, and in other cases the patient may not be able to swallow a whole tablet.

But unless certain precautions are taken, tablet splitting can lead to medication errors. If the patient is splitting the tablets at home, he or she can become confused about the dose. Patients often forget to split their tablets, or they can split them again after they've been pre-split in the pharmacy. Some patients may not have the visual acuity or motor skill to do the splitting properly. Even when split well, the pieces can crumble or be uneven in size.

Patients may not be the only possible source of error. When the prescription is written as "1/2 tablet," the pharmacist can confuse this with "1-2 tablets," which could lead to a fourfold overdose.

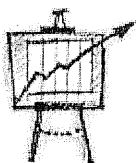
ISMP suggests several ways to prevent errors with tablet splitting:

- Be sure that the tablet in question is suitable for splitting. If in doubt, check with the manufacturer.
- Ensure the patient has the understanding, skill and motivation to split the tablets. You may have to enlist a family member or caretaker to do this.
- If the tablets are to be split at home, provide the patient or family with a tablet splitter to improve accuracy.
- For inpatients, the pharmacy staff should dispense the tablets already split, rather than relying on nurses to do this on the floor.
- Prescribers should order the strength in milligrams when possible, to avoid misreading an order for "1/2 tablet" for "1-2 tablets."

Additional Information:

ISMP Medication Safety Alert. Tablet Splitting: Do it only if you "half" to and then do it safely. May 18, 2006.
<http://www.ismp.org/Newsletters/acutecare/articles/20060518.asp>

FDA Patient Safety News is available at www.fda.gov/psn



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"Pill Splitting" - Is It Legal? Is It Covered By Malpractice Insurance?

By Kenneth R. Baker, B.S.Pharm., J.D.
Vice President, General Counsel
Pharmacists Mutual Insurance Company

Several pharmacists have called asking these questions regarding "pill splitting".^[1] These pharmacists have indicated they are receiving requests from third party payers and from physicians, and occasionally from patients, to split some prescription medications prior to dispensing. In most cases the questions involve unscored tablets and in most cases, the reason for the request is to save money for the patient or the third party payer.

The real question for the pharmacist involves two considerations – the law and pharmacy judgement. Whether the pharmacist can "split" unscored tablets is determined by both considerations. In most states, at present, there are no laws or pharmacy regulations specifically forbidding "pill splitting", although there are warnings in pharmacy literature discouraging it. The pharmacist, asked to "split" tablets, needs to know if there is a legal restriction in the state in which he or she practices.

As part of the legal consideration, the manner in which the prescription is written becomes important. If the prescription indicates "DrugX, 50 mg", it must be filled exactly as written. In order to fill the prescription with a split DrugX, 100 mg tablet, the pharmacist must be able to split the tablet in a manner that assures each one-half contains exactly 50 mg of DrugX. Therein lies the problem. An unscored tablet cannot be divided exactly equally. Without the prescriber's specific orders to split the tablet, the prescription may not have been filled as ordered. This may be a violation of the state pharmacy practice act.

Even if the doctor does order or approve the split "into two parts of approximately the same strength", the pharmacist's act of splitting the tablets into strengths commercially available, may arguably amount to illegal compounding under Section 503A^[2] of the FDA Modernization Act of 1997. It may be argued that the compounding definition is broad enough to include preparation of a dose by splitting the tablets. If so, and if the resulting one-half dose is commercially available, the action could be interpreted as a violation of the federal statute which says: "*A drug product may be compounded . . . if the licensed pharmacist . . . (D) does not compound regularly or in inordinate amounts (as defined by the Secretary) any drugs products that are essentially copies of a commercially available drug product.*"^[3] (emphasis added).

Even if the law allows it, the decision must be made by the pharmacist based upon professional judgement and patient best interest. Generally speaking, pill splitting by the pharmacist is not a good idea and should be avoided, absent some overriding consideration for a particular patient.

If the pharmacist knows a patient is going to split unscored tablets, the law will have little to say about the patient's actions, but the pharmacist

should consider the application of pharmaceutical care to the situation. The pharmacist should: warn the patient about the inexactness of the resulting half table dosage; warn the patient of the possible effects of an inexact dose – too high or too low; and tell the patient to let his prescriber know that he/she is splitting tablets. The pharmacist should also consider what other advice he/she should give. The pharmacist should be certain the patient understands that while cost is a legitimate consideration, it should not be the primary consideration.

The second question -- “Is it covered?” – is a product of the first. Most policies contain an exclusion similar to this: *“This policy does not apply to . . . damages caused by your willful violation of a regulation or statute pertain to the practice of pharmacy . . . committed by you or with your knowledge or consent.”* (emphasis added). If the action of “pill splitting” is known by the pharmacist to be a violation of the law, the exclusion applies. If however, the pharmacist does not willfully violate the law, even if it later becomes apparent it is a violation, the policy would cover, in spite of the exclusion, even if the action is unwise. A board of pharmacy or a court, however, may not care if the pharmacist was ignorant of the law and will not excuse the pharmacist who pleads, “I did not know about that rule”.

The ultimate bottom line for the professional pharmacist is – if it is not good pharmacy practice, don’t do it.

^[1] See, www.health24news.com, Holton, N., Pill Cutting for Cost Cutting, (March 2000, *Health24*)

^[2] 21 U.S.C. 353 § 503A

^[3] 21 U.S.C. 353 § 503A (b) (1)(D).

This article discusses general principles of law and risk management. It is not intended as legal advice. Pharmacists should consult their own attorneys and insurance companies for specific advice. Pharmacists should be familiar with the policies and procedures of their employers and insurance companies, and act accordingly.



Pill Splitting Could Help You Cut Drug Costs

From Mark Cichocki, R.N.,
Your Guide to HIV / AIDS.

FREE Newsletter. [Sign Up Now!](#)

It's no secret that the cost of prescription drugs is getting out of hand. Even people lucky enough to have drug coverage find that their monthly copays can run into the hundreds of dollars each month. A simple idea may be a way to cut those copays in half.

Many drug insurances and employers are promoting a concept called pill splitting. Here's the idea. Many medications come in different doses. Let's use the drug [Lipitor](#) for instance. Lipitor is used to control cholesterol. It comes in 20mg and 40mg tablets. Traditionally, people needing a dose of 20mg per day would take one 20mg tablet per day; 30 tablets in a month. Most drug insurances will charge the person a copay; the amount not covered by the insurance. For our example we will say the copay is \$20. So each month, the person gets his 30 Lipitor tablets at the pharmacy and pays the \$20 copay. The quantity of 30 tablets will last him 30 days.

Pill splitting can decrease the copay by half. Here's how. In our example, our patient takes one 20mg tablet of Lipitor each day, for a total of 30 per month. Pill splitting has the patient get Lipitor 40mg tablets and has him split the pill in half to get his 20mg dose each day. The same 30 tablets now last 60 days because only 1/2 the 40mg tablet is being taken each day to get the 20mg dose. The copay for the 30 tablets will still be \$20 but he will only have to get the prescription filled every other month, thus saving him \$20. Let's look at it a different way:

- Lipitor 20mg per day - (1) 20mg tablet each day - 30 tablets per month with a copay of \$20
- Lipitor 20mg per day - (1/2) 40mg tablet each day = 20mg dose - 30 tablets now last 60 days for the same \$20 copay.

Pill splitting can be an easy way to save some money but unfortunately it doesn't work for everyone. For example:

- Capsules can't be split so any medicine that is in a capsule form can't be taken using pill splitting.
- HIV meds are single dose medicines which mean there is no way to split a dose and still get the proper amount of medicine.
- Only tablets that have a scored line down the center can be split or broken in half.

Before you use pill splitting to save some money, check with your doctor and your pharmacist to see if the medicines you are taking can be split. If your doctor okays pill splitting, purchase a pill splitter; a small, inexpensive device that will make breaking a pill in half easy and accurate. While many pills can be split by hand, doing so leaves room for error and increases the incidence of inaccurate breaks. Using a pill splitter will allow you to break your pills accurately, assuring you get the proper dose of medicine.

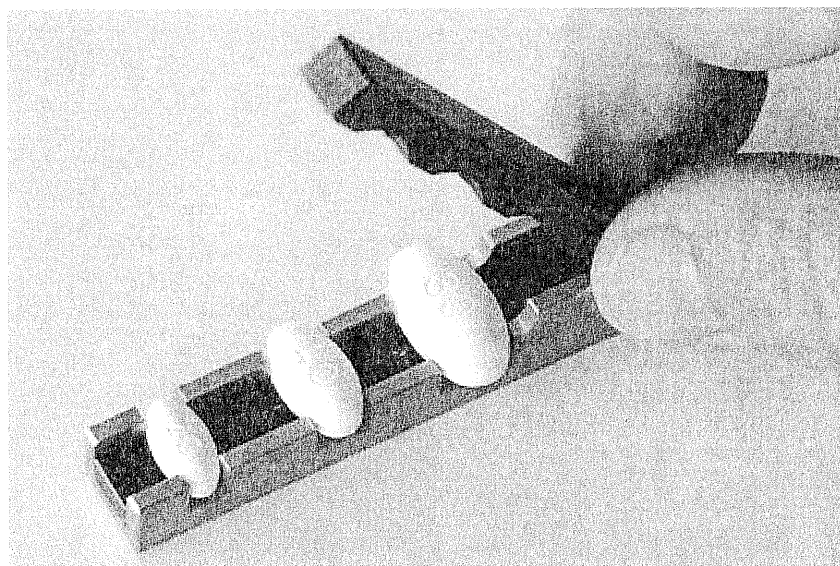
Ask your doctor and your pharmacist today if pill splitting will work for you.

This About.com page has been optimized for print. To view this page in it's original form, please visit:
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Swiss Pill Cutter for Lipitor

- Exclusive Lipitor Pill Cutter design insures accurate cut
- Cuts 80 mg, 40 mg and 20 mg Lipitor tablet in half and 80 mg tablet into quarters
- Precision machined from tool quality steel alloy



Lipitor is the largest selling prescription drug in the World at around \$11 billion in annual sales. Many Lipitor users and many physicians who prescribe Lipitor do not realize that the cost to the individual is around **\$1,300 per year** regardless of whether they need the 80 mg tablet, the 40 mg tablet, the 20 mg tablet or the 10 mg tablet. (The 10 mg tablet is slightly cheaper.)

No wonder so many Lipitor users ask their physician to prescribe a larger dose than they need and then try to cut the tablet in half or quarters. Swiss Precision Cut has received many requests for a pill cutter that will accurately and precisely cut Lipitor into halves or quarters.

Most of the emails we receive are from users who have tried unsuccessfully to cut Lipitor with a sharp knife or a single edge razor blade. Many have also tried a typical plastic pill cutter that is available at the drugstore or is provided free of charge by an insurance company, HMO or Internet pharmacy. Although many inexpensive or free pill cutters are available, they apparently don't work very well. The most common complaint is that the Lipitor tablet cuts unevenly or crumbles most of the time.

Inexpensive pill cutters are designed to cut a large variety of pills, and are not specific toward size or shape. They work well on pills or tablets that have a soft coating or are serated to facilitate easy cutting. Aspirin is a good example of this type of pill.

All of the pill cutters that we have seen are plastic and usually have a single edge razor blade embedded in the cutting edge. This razor blade

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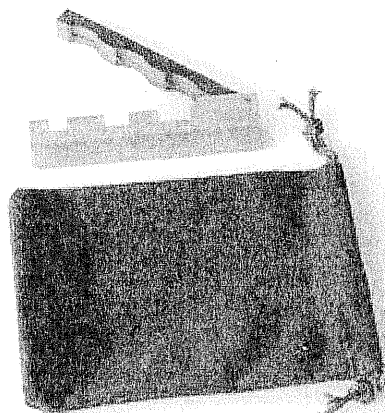
may work satisfactorily on soft pills for a while, but like any other razor blade, it dulls quickly with use.

The Swiss Pill Cutter for Lipitor is radically different from any other pill cutter on the market. It is precision machined from tool quality steel alloy rather than molded plastic. The cutting edge will never dull and never needs to be replaced no matter how many times it is used.

Another significant feature is that there is a separate built-in pill bed for the 80 mg tablet, the 40 mg tablet, and the 20 mg tablet. This is extremely important because it allows the user to split different size pills as the doctor prescribes different doses while determining the optimum dose.

Lipitor normally takes 4 or 5 weeks to stabilize on a new dosage. Your physician might start with the 10 mg tablet and then prescribe the 20 mg tablet a month later if the desired cholesterol objectives are not achieved. Since the Swiss Pill Cutter for Lipitor can handle all sizes, the savings are always there without having to buy another pill cutter.

The Swiss Pill Cutter for Lipitor comes with a velour pouch, perfect for pocket or purse. At \$49.00 plus \$4.00 shipping anywhere in the World, the Swiss Pill Cutter for Lipitor pays for itself the first month it is used. **The typical user can save \$328 - \$1,001 per year.**

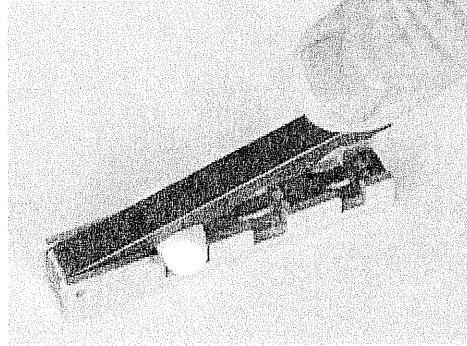


If you are not satisfied with the Swiss Pill Cutter for Lipitor for any reason, return it within 90 days for a full refund.

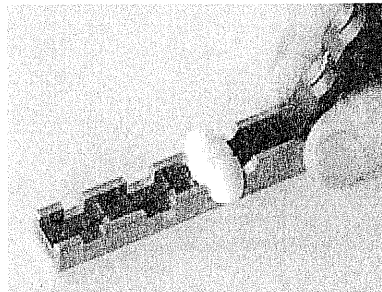
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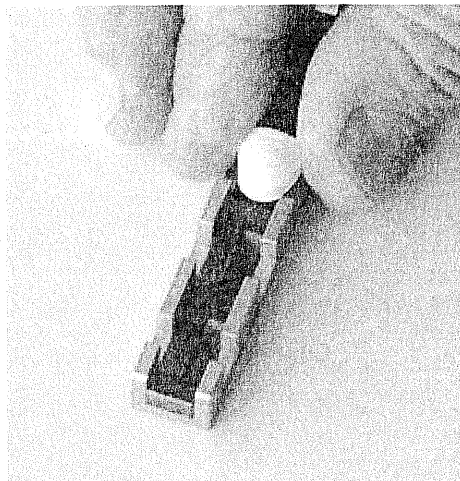
How the Swiss Pill Cutter for Lipitor Works



To cut the Lipitor tablet in half, place it in the pill bed, put on table or counter, and push down with thumb.



To cut the half Lipitor tablet into quarters, hold the half pill in the pill bed with your thumb and forefinger.



Place Cutter on hard surface and push down with thumb.

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Pill-Splitting: How To Correctly Split A Pill

Researchers at the Veterans Administration Medical Center in Asheville, N.C., studied patients to determine how effectively they were able to cut various types of splittable pills, and whether arthritis, a common disorder of aging, hampered that ability.

"Patients' perceptions of having conditions that affect their hands didn't seem to be as big a problem as we thought," said Brian Peek, the clinical pharmacist who led the VA study. "We knew some of them had arthritis, and that did not turn out to be a significant predictor" in accurately halving tablets.

The researchers also wanted to know if detailed instructions from pharmacists made people better pill splitters.

"We had them use two fairly common splitting devices," Peek said of a hinged cutter and a special razor blade, both of which can be purchased at pharmacies.

All too often, Peek said, patients buy splitters from pharmacies and never ask for individual instruction. He and his colleagues set up the study to take that reality into account.

In the analysis, 30 men between the ages of 50 and 79 were assigned to rotating groups: splitter A with instruction and splitter A without instructions. The two groups used the hinged cutting device. There were also two splitter B groups, with and without instructions, using the razor.

Participants who were in the "instructed" groups were read how to split pills, followed by a demonstration of the practice. Pill splitters in the instructed groups were allowed time to ask questions. The groups receiving no instruction were simply read general information about the study itself.

Patients then were asked to split 14 tablets of each of these types: flat round tablets, irregularly shaped tablets, small oblong tablets and large oblong ones. Tablet weight before and after splitting was determined by an analytical weight.

In the end, regardless of group, researchers found patients' tablet-splitting resulted in dosage deviations between 9 percent and 37 percent from those intended. Peek said about 47 percent of patients in the study

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Pill-Splitting: How To Correctly Split A Pill

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reported experience with having split pills on their own. And those with experience, regardless of instruction, were most accurate at splitting flat, round tablets. More deviations in dosage were found with the more irregularly shaped pills.

However, Peek added that an approximate deviation of as much as 10 percent may not be clinically significant with many medications that are split. Larger deviations in the study could prove hazardous for medications with a "narrow therapeutic index." Such an index, Peek said, refers to medications that can have under- or overdoses when inaccurately cut.

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Warfarin, a powerful blood thinner, is a prime example of a narrowly indexed drug. Cutting away even slightly more than half of the drug eliminates the medication's therapeutic ability, leaving the patient vulnerable to dangerous clots. When too much of the medication is left on the split "half," patients are in danger of hemorrhaging.

"We hope that this study, along with others in the medical literature, will help health care providers make decisions about tablet splitting, especially when tablet-splitting is looked at as an option," Peek said.

Warning: Do not make any changes in your medications or the way you take your medications without first talking it over with your doctor.

RELATED LINKS AND INFO

[A Look At Pill Splitting](#)

[The Divide Over Pill-Splitting](#)

[Psychiatric Pills With Splitting Potential](#)

For more information about pill splitting, go to the American Society of Consultant Pharmacists Web site.

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Splitting Pills to Save Money

Jane picked up her medication from the pharmacy. When it was time to take her pill, she split it into two halves with a small device from the drug store. The next day when it was time to take her pill, she took the other half of the pill she had split the day before. She did this every day for two months, which saved her the co-pay she would have paid for the second month.

Jane discussed this with her doctor who said it would be OK to take her medicine this way. She also told her pharmacist so he would not alert Jane about a refill she didn't need. Her pharmacist also helps Jane avoid mistakes with her medication.

Splitting her pills worked for Jane but it may not work for you. Some medicine just cannot be split.

Here are some guidelines that you should know before you speak with your doctor.

Things to look for that probably mean your medicine cannot be split:

- The medicine is in capsule or liquid form. Splitting only works with pills or tablets.
- The pill crumbles or does not split cleanly. This would mean that you would not get all of your medicine.
- The medicine is time-released. This means that your medicine is manufactured so that it works slowly over a specific number of hours.
- The tablet has a coating or film, usually because the pill without it would have an unpleasant taste but or because it makes the medicine easier on your stomach.
- The tablet or pill is not scored, which means that it doesn't have a slight groove or indent down the middle. There are some exceptions to this.

If your medicine passes the test, there are still some questions to ask yourself:

- **Can I split all my pills at once?** Not always - some pills can only be split one at a time. Being exposed to air makes some medicine less effective.
- **Is this just too complicated?** You may be taking several medications

and the saving is not worth the hassle for you.

- **Do vision problems make this too difficult?** Some pills are very small and splitting them may make them just too small to handle.

Jane is on a tight budget and is happy with the small savings she gets from splitting her pills. She uses an inexpensive device she buys at the drug store, which is much safer than trying to use a knife and cutting board.

Always discuss any changes in the way you take your medicine, such as splitting the pills, with your doctor.

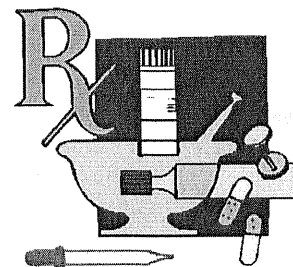
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<http://pharmacy.orst.edu/>

Spring 2001

Chronic Insomnia: Misuse of Hypnotic Therapy in Oregon

By: Ann Hamer, Pharm.D.

Motivated by concerns of hypnotic misuse, OMAP conducted an internal review of hypnotic prescribing patterns. Specific areas of concern were chronic hypnotic use, excessive dosing in the elderly and duplicate therapy. A review of all patients filling two hypnotic prescriptions on the same day discovered that at least 19 patients received both Ambien (zolpidem) and Sonata (zaleplon) at the same time during the first 9 months of last year. It is interesting to note that despite the fact that insomnia guidelines recommend only short-term (7-10 days) hypnotic drug therapy, the average duration of sedative use in the year 2000 was 3 to 6 months.

Of 525 patients receiving zaleplon therapy, approximately 12% received higher than the recommended dose of 10 mg qhs (range: 2-60 mg). Out of 264 patients on triazolam therapy, approximately 14% received more than 0.25 mg qhs (range: 0.055-2.0 mg). Results showed 81 patients over the age of 64 (over 50% of this group) received excessive doses.

INTRODUCTION – Sleep is a basic requirement. Without the benefit of a good night's sleep, a person may experience daytime sedation, increased levels of anxiety, depression and medical illness, decreased productivity and an increased propensity for accidents. Up to one-third of primary care patients experience sleep difficulties. Of those patients, approximately 10% have chronic insomnia, or the subjective experience of an inadequate quantity or quality of sleep that has persisted for at least one month.^{1,2} The following is a review of the appropriate diagnosis and treatment of chronic insomnia.

DIAGNOSIS – Idiopathic chronic insomnia is very rare. Insomnia, therefore, should be considered a symptom; a symptom of an underlying pathological condition. The identification and elimination of all possible causes should take precedence. Table 1 provides a list of common causes of insomnia in the primary care patient.

To best diagnose and treat insomnia, it is critical to perform a thorough clinical interview. This should include a review of medical conditions, a complete medication history, interviews with bed partners, and data from a sleep diary, including sleep latency, sleep duration, number of awakenings and subjective assessments of sleep quality and quantity.

TREATMENT–NONPHARMACOLOGIC THERAPY – The first step in the treatment of chronic insomnia should be the elimination of the causative

factor(s) if possible. Underlying medical conditions should be treated appropriately. For example, an underlying depressive disorder should be treated with an antidepressant.

Nonpharmacologic therapy, consisting of both behavioral and cognitive changes, is a reasonable second step. Nonpharmacologic interventions for insomnia are primarily short-term cognitive-behavioral therapies aimed at alleviating the factors that are presumed to perpetuate insomnia. In other words, they attempt to modify poor sleeping habits, reduce autonomic and cognitive arousal, alter dysfunctional beliefs and attitudes about sleep, and educate patients about healthier sleep practices.³ The results of 2 meta-analyses of behavioral treatments suggest that 70-80% of patients with primary insomnia experience improvements.⁴

Table 1. Common Causes of Insomnia

Drugs	Medical Conditions
<ul style="list-style-type: none">• OTC medications (eg, pseudoephedrine)• Nicotine• Prescription drugs<ul style="list-style-type: none">– methylphenidate, pemoline– theophylline– albuterol– quinidine– diuretics– dextroamphetamine– phenylephrine– SSRIs	<ul style="list-style-type: none">• sleep apnea, restless leg syndrome• pain• thyrotoxicosis• drug/alcohol intoxication or withdrawal• dyspnea from any cause• nocturnal myoclonus
Psychologic Causes	Environmental Causes
<ul style="list-style-type: none">• depression• anxiety• conditioning• mania or hypomania	<ul style="list-style-type: none">• temperature• noise• eating, exercise, caffeine or alcohol use before bedtime• jet lag• shift work• daytime napping

Sleep hygiene is a necessary component of all insomnia interventions, and may be sufficient as a stand-alone treatment. Other nonpharmacologic therapies include stimulus control, progressive muscle relaxation and sleep restriction. See Table 2 for a description of various nonpharmacologic interventions.

There are at least 15 studies available that have compared 2 or more of the following nonpharmacologic interventions: stimulus control, relaxation, sleep restriction and sleep hygiene education. Only 5 studies have found a statistically significant difference between response to these interventions; with stimulus control and sleep restriction being more effective than relaxation and sleep hygiene education.³ Published studies show that while hypnotic drugs may produce faster sleep improvements, particularly in the first few days, behavioral methods such as relaxation and sleep hygiene education have comparable effect in the intermediate term and are clearly superior in long-term therapy. Even those patients on long-term combination therapy (hypnotic drugs plus behavior therapy) do not do as well as those with behavior therapy alone.³

There are at least 15 studies available that have compared 2 or more of the following nonpharmacologic interventions: stimulus control, relaxation, sleep restriction and sleep hygiene education. Only 5 studies have found a

• • **CHRONIC INSOMNIA** - continued on page 2

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Table 2. Nonpharmacologic Therapies for Insomnia

THERAPY	DESCRIPTION
Sleep Hygiene	<ul style="list-style-type: none"> • Limit/stop the use of nicotine, alcohol and caffeine • Keep regular sleep and wake times, even on days off from work • Exercise regularly, but no later than late afternoon or early evening • Only use the bed for sleep or sex • Avoid daytime naps • Avoid poor sleep environments • Do not eat heavy meals before going to bed
Stimulus Control	<ul style="list-style-type: none"> • Patient uses a set of instructions designed to establish in the bedroom cues for sleep instead of wakefulness
Sleep Restriction	<ul style="list-style-type: none"> • Length of time spent in bed is limited to create partial sleep deprivation, resulting in deeper, more continuous sleep
Relaxation Training	<ul style="list-style-type: none"> • Biofeedback, autogenic training, progressive muscle relaxation and hypnosis
Cognitive Therapy	<ul style="list-style-type: none"> • Psychotherapy aimed at changing the patient's perception of the insomnia

statistically significant difference between response to these interventions; with stimulus control and sleep restriction being more effective than relaxation and sleep hygiene education.³ Published studies show that while hypnotic drugs may produce faster sleep improvements, particularly in the first few days, behavioral methods such as relaxation and sleep hygiene education have comparable effect in the intermediate term and are clearly superior in long-term therapy. Even those patients on long-term combination therapy (hypnotic drugs plus behavior therapy) do not do as well as those with behavior therapy alone.³

To improve the outcome of nonpharmacologic therapy, patients should be thoroughly educated about each technique and appropriate expectations. Table 3 provides some useful online resources for patients.

Table 3. Patient Resources

Muscle Relaxation Techniques <ul style="list-style-type: none"> • http://ourworld.compuserve.com/homepages/har/relax.htm • http://www.mckinley.uiuc.edu/health-info/stress/rela-exe.html
Sleep Hygiene <ul style="list-style-type: none"> • http://www.thesleepsite.com/hygiene.html

TREATMENT-PHARMACOLOGIC – Pharmacologic therapy is indicated when nonpharmacologic approaches are insufficient to relieve the insomnia. When used in combination with behavioral therapy, patients tend to respond well with long-term benefits.³ In general, hypnotic drug therapy should be used intermittently as needed and for a limited duration (• 8 weeks).

Barbiturates and Other Older Hypnotics – These agents have fallen out of favor due to their high propensity for adverse effects, tolerance, and dependence.

Antidepressants – While there are few data that focus on the use of antidepressants in primary insomnia, these agents have been used successfully to treat insomnia. At low doses, these agents have minimal side effects and are inexpensive. It is recommended that practitioners start with a low-dose tricyclic antidepressant (eg, amitriptyline) or trazodone. When prescribing tricyclic antidepressants (TCAs), it is important to consider their safety. In low doses (10-25 mg amitriptyline), these drugs are typically well tolerated. Elderly patients are more susceptible to anticholinergic side effects and should be prescribed lower starting doses of both TCAs and trazodone. Side effects become more prominent with higher doses such as those used in the treatment of depression. TCAs can be fatal in overdose. Caution should be used when prescribing TCAs with medication that could inhibit their metabolism (ie SSRIs). Priapism, a rare side effect of trazodone, can be of concern with male patients taking doses greater than 150mg. SSRIs are not recommended for use in patients with primary insomnia; they may induce or worsen pre-existing sleep disorders.

Benzodiazepines – Benzodiazepines have traditionally been recognized as the mainstay of therapy for the treatment of insomnia. Benzodiazepines, like all sedating medications, should not be used if there is any suspicion of obstructive sleep apnea. Prior to selecting a particular

benzodiazepine, several factors need to be taken into consideration including: patient's age, liver function, pharmacokinetics of the drug, specific insomnia symptoms, and substance abuse history. Lorazepam, temazepam and oxazepam are considered the benzodiazepines of choice in the presence of hepatic dysfunction. These drugs undergo glucuronide conjugation and their half-lives are only slightly altered by hepatic disease. Elderly patients should not receive long-acting benzodiazepines such as diazepam, clonazepam or flurazepam. Due to reduced liver metabolism and drug accumulation, such agents have been linked to increased falls, hip fractures and motor vehicle accidents.⁴ For further information on treating insomnia in the elderly, see the final section on treating insomnia in special populations.

Triazolam (Halcion) is a benzodiazepine with a short 6 to 7 hour duration and quick 15 to 30 minute onset of action. Its amnestic side effects have received a lot of bad press. Like any benzodiazepine, triazolam should be used cautiously. It should be given in small doses (0.125 mg to 0.25 mg) and for short periods of time (7 to 10 days). Interestingly, triazolam and zolpidem (a newer nonbenzodiazepine hypnotic) have been documented to cause similar impairment of memory and abuse potential.^{5,6}

Benzodiazepines are associated with many adverse effects, particularly with the use of high doses long-term. These agents should be dosed intermittently, for a limited duration and at the lowest dose possible.^{1,7} Tolerance and dependence may occur after only 1 to 2 weeks with short and intermediate-acting agents.⁸ Benzodiazepines should be withdrawn gradually (eg, 25% per week) to avoid withdrawal reactions (including seizures) and rebound insomnia. Patients who have been on benzodiazepines long-term will require a slower, more individualized taper.

Nonbenzodiazepine Hypnotics – Two newer nonbenzodiazepines, zolpidem (Ambien) and zaleplon (Sonata), are thought to be selective for the BZ-1 receptor subtype. Both agents are indicated for the short-term treatment of insomnia. An advantage of these agents over some benzodiazepines is their rapid onset of action and short elimination half-life. Zaleplon, with an average onset of activity of 15 to 20 minutes, can be dosed during the middle of the night with little risk of daytime sedation. It should be recognized that the average onset of action for triazolam is 15 to 30 minutes as well. Drawbacks to the nonbenzodiazepine hypnotics include impaired memory and concentration, headache, GI upset, drug tolerance, cost and lack of efficacy in some patients.

According to the manufacturers of both zolpidem and zaleplon, duration of therapy should be limited to 7-10 days.^{9,10} There are no published data available that support the use of either agent long-term. In fact, in two unpublished controlled trials, it was determined that the beneficial effects of zolpidem are only short term, with tolerance developing by the fifth week of use. Chronic standard zolpidem therapy (5-10 mg qhs) is considered to be no better than placebo.⁹

Only two 4-5 week zaleplon trials have been performed in chronic insomniacs. Results of these studies showed that while zaleplon significantly decreases time to sleep onset or sleep latency (10-20 minutes) compared to placebo, it does not have any effect on sleep duration or number of awakenings.¹⁰ Other sleep laboratory studies performed in outpatient chronic insomniacs have had a maximum duration of 28 days. A summary of these findings demonstrated that zaleplon significantly reduced latency to persistent sleep compared to placebo during the first two nights of therapy only.¹⁰ Zaleplon comparative efficacy trials have failed to clearly demonstrate an advantage over the short-acting benzodiazepine triazolam.¹¹







Nonbenzodiazepines should only be used in patients with primary sleep latency disorders. All agents within this class have failed to demonstrate consistent improvements in sleep duration, number of awakenings, and overall sleep quality. There are no distinct advantages of these agents over conventional benzodiazepines (such as triazolam). Evidence does not support the long-term use of nonbenzodiazepine hypnotics.

Natural Products – There are many over-the-counter herbal products that are touted as sleep aids. Valerian (from the underground parts of *Valeriana officinalis*) causes both CNS depression and muscle relaxation. It is reported to decrease sleep latency and improve subjective sleep. There are few studies available that provide evidence for the hypnotic efficacy of valerian. In addition,

• • **CHRONIC INSOMNIA** - continued from page 2

there are safety concerns associated with its use. Based on the 1994 Dietary Supplement Health and Education Act (DSHEA), herbs, vitamins, minerals and amino acids can be marketed as dietary supplements. As such, herbal manufacturers are not required to provide safety, purity and efficacy data. As a result, the content and purity of herbal preparations may vary from batch to batch. Of specific concern with valerian, it is feared that valepotriates in high concentration may be cytotoxic.⁸ More data must be collected on this drug before its role in insomnia can be defined.

Table 4. Data From Two Controlled Long-Term Zolpidem Trials.⁹

SLEEP CHARACTERISTIC	WEEK ONE	WEEK TWO	WEEK THREE	WEEK FOUR	WEEK FIVE
Study #1: 10 mg qhs for 5 weeks (arrow indicates when efficacy is greater than placebo)					
Sleep Latency					
Sleep Efficiency					
Number of Awakenings	no better than placebo during entire study duration				
Study #2: 10 mg qhs for 4 weeks (arrow indicates when efficacy is greater than placebo)					
Sleep Latency					
Total Sleep Time					
Number of Awakenings					
Sleep Quality					

Melatonin, a neurohormone synthesized from tryptophan and secreted by the pineal gland, has recently gathered a lot of press as a sleep aid. Melatonin's role in regulating the sleep-wake cycle, particularly in jet-lag, is well documented. Low-dose melatonin as a hypnotic is considered to be variably effective. Data suggest that the efficacy of melatonin is affected by time of administration (best if 2 hours before bed), product bioavailability (not FDA regulated), and length of therapy. Melatonin appears to be more effective with repeated doses.⁸ It should be stressed, however, that ongoing need for a sleep aid should be thoroughly evaluated to rule out underlying causes. Further safety and efficacy data are needed.

Recommendations for the Pharmacologic Treatment of Insomnia

- Nonpharmacologic therapy is a critical addition to all treatment strategies.
- Pharmacotherapy should not be considered the mainstay of treatment for chronic insomnia.
- If pharmacotherapy is necessary, sedating antidepressants are reasonable first choices.
- All sedative hypnotics should be given for a limited duration.
- If a longer duration is necessary, as-needed intermittent therapy is as effective as chronic therapy.
- Zolpidem and zaleplon are not recommended beyond 10 days of therapy.
- Drug therapy should be withdrawn slowly to avoid rebound insomnia.

Table 5 provides a summary of the drug classes used as sedative/hypnotics.

TREATING INSOMNIA IN SPECIAL POPULATIONS**Psychiatric Illness**

Insomnia and Depression – Sleep disturbances are a common part of depressive disorders, and as such, are included in all contemporary sets of diagnostic criteria for major depression. It is thought that insomnia in depression is caused by a dysfunction of the serotonin systems², and that the stimulation of serotonin-2 receptors causes changes in sleep architecture seen with selective serotonin reuptake inhibitors (ie, fluoxetine, sertraline, citalopram, paroxetine and fluvoxamine) and serotonin-norepinephrine reuptake inhibitors (ie, venlafaxine).¹³ Management of depression with these agents may necessitate the short-term use of coprescribed low-dose trazodone or other sedative. With continued use of

SSRIs, symptoms of insomnia should improve, enabling the discontinuation of dual therapy. An alternative approach to the management of comorbid depression and insomnia is the use of antidepressants that *block* the serotonin-2 receptor, such as mirtazapine or nefazodone. Both of these agents are equally effective antidepressants compared to SSRIs and they alleviate insomnia and improve sleep architecture. Antidepressants with serotonin-2 blocking properties are good single treatment options for depressed patients with marked insomnia.¹³

Table 5. Pharmacologic Therapies for Insomnia

DRUG	ADVERSE EFFECTS	EFFECT ON SLEEP STRUCTURE ^c	COST FOR 10 DAY TREATMENT (\$)*
BENZODIAZEPINES			
clonazepam (Klonopin)	rebound insomnia daytime sedation headache	• sleep latency ^a • total sleep time ^b	\$6.80
temazepam (Restoril)	confusion hypotension hangover dependence	• delta sleep ^c • REM sleep ^d	\$7.00
triazolam (Halcion)	withdrawal respiratory depression		\$5.90
NONBENZODIAZEPINE HYPNOTICS			
zolpidem (Ambien)	headache N/V confusion dizziness tolerance/withdrawal	• sleep latency • total sleep time • delta sleep • REM sleep	\$22.40
zaleplon (Sonata)	headache somnolence dizziness tolerance/withdrawal	• sleep latency • total sleep time • delta sleep • REM sleep	\$22.30
ANTIDEPRESSANTS			
amitriptyline (Elavil)	drowsiness CV effects seizures	• sleep latency • delta sleep	\$0.90
imipramine (Tofranil)	hypotension anticholinergic effects	• REM sleep	\$4.50
trazodone (Desyrel)	dry mouth dizziness drowsiness N/V hypotension	• sleep latency • total sleep time • delta sleep • REM sleep	\$2.80
OVER-THE-COUNTER AGENTS			
diphenhydramine (Nytol, Sominex)	dyskinesias headache sedation	• sleep latency • total sleep time	\$1.70
doxylamine (Unisom)	dry mouth weight gain tolerance	?delta sleep ?REM sleep	\$3.40

*Based on AWP from Red Book Update, January 2001; 20(1).

a. Sleep latency = time to onset of sleep

b. Total sleep time = duration of sleep

c. Delta sleep = slow-wave, deep, restorative sleep

d. REM sleep = Rapid Eye Movement sleep

Regulation of the Sleep-Wake Cycle in Bipolar Affective Disorder – There is some evidence to suggest that the disruption of sleep in bipolar patients may precipitate a manic episode.^{14,15} Disrupted sleep schedules may occur as a result of psychosocial stressors such as jet lag, school examinations or rotating work shifts. Sleep is typically considered a priority in the treatment of manic patients, thus necessitating the use of a short-term sedative/hypnotic. There are no data regarding the need, efficacy or adverse effects of chronic sedative administration in this patient population. It is therefore recommended that sedative/hypnotics be prescribed on an acute basis only.

Elderly – Sleep structure changes with age. The biphasic propensity for sleep seen in young adults becomes multiphasic in the elderly. Studies have shown that in the elderly, sleep latency increases and sleep efficiency decreases, as does time in deep sleep.¹⁶

Treatment of insomnia in the elderly adult should follow guidelines similar to those of younger adults. Good sleep hygiene and stimulus control education

• CHRONIC INSOMNIA - continued from page 3

is imperative. Daily exercise and exposure to daylight can help reinforce the circadian cycle. Select patients may require the use of a sleep-promoting medication. Over-the-counter medications (antihistamines) are rarely recommended due to their anticholinergic side effects. Low-dose antidepressants (such as trazodone) are an excellent first choice, particularly in patients with comorbid depression. Low-dose short-acting benzodiazepines are also a reasonable choice. Dosing of these agents is generally one-half the dose for younger adults. Caution should be used when prescribing medications that are affected by poor renal or hepatic function. Again, long-acting benzodiazepines should be avoided in the elderly.

CONCLUSION — Chronic insomnia is rarely a primary disorder. More commonly, it is a symptom of an underlying medical or psychiatric illness. A thorough evaluation of the patient is warranted prior to the diagnosis of chronic idiopathic insomnia. Nonpharmacologic therapy is considered first-line in all patients. Short-term sedative/hypnotics may be required in certain patients in whom the insomnia does not resolve. If these agents are used longer-term, they should be prescribed intermittently. Chronic use of sedative/hypnotics is strongly discouraged. Agent selection should be based on symptoms, side effects, efficacy studies and cost.

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Controlling The Rising Cost of Medications

By: **Lori Syed, Pharm.D. & Dean Haxby, Pharm.D.**

Health care costs have been increasing at an alarming rate. One of the primary factors driving this increase is spending for prescription drugs. While prescription drugs account for approximately 9% of total health care costs, they were responsible for 44% of the total increase in 1999. In 2000, expenditures for prescription drugs increased by 19%. A March 2000 study conducted by the University of Maryland projects that prescription drug costs may increase by as much as 18% a year over the next 5 years. This means that by 2004, prescription costs would be double that spent in 1999. As spending on prescription drugs makes up a larger portion of health care costs, fewer resources are available for other health care services, including provider reimbursement.¹

The rising cost of pharmaceuticals can be attributed to several key factors. In 2000, an increase in the number of prescriptions written caused 42% of the rise, while a shift to higher cost drugs accounted for 36%. Other factors accounting for the remainder of the rise include increased prices of existing drugs and longer durations of therapy. It is clear that aggressive marketing

to providers and consumers is reaping rewards for the pharmaceutical manufacturers. While some newer drugs offer advantages over older, existing agents, many do not. Yet new drugs are aggressively marketed, regardless of their merits.² Fortunately, there are a number of tactics clinicians can take to improve the cost effectiveness of their prescribing. The purpose of this article is to point out strategies that can help contain prescription drug costs, while maintaining quality of care.

Become Better Informed About Drug Prices — It is very difficult to make cost effective choices without knowing the relative cost of drugs. Become familiar with the costs of the drugs that you commonly prescribe. A recent study demonstrated that lack of provider knowledge of drug prices was a major contributor to higher cost prescribing. Sources of drug pricing information include pharmacists, managed care prescribing guides, the Medical Letter and the Red Book.

Frequently Review Patients' Drug Profiles and Avoid Polypharmacy — Be sure that each drug prescribed has an indication, and look for those indications which have resolved or changed. This is especially important following a hospital admission. Try to limit the number of medications prescribed. As the number of prescribed medications increases, the chance for adverse effects, drug interactions or non-adherence increases. When assessing the lack of effect of a drug, first assess compliance, then consider if an adequate dose has been tried. If it becomes necessary to change the regimen, consider discontinuing the product and changing to a different medication, rather than just adding another medication onto the regimen. Avoid treating side-effects with more drugs. It is important for physicians to evaluate for side-effects of the medications they prescribe, and for pharmacists to discuss effects and key monitoring parameters with patients. Finally, when changing or discontinuing medications, be certain that a patient clearly understands the change, and if necessary, understands to stop taking the previous medication.

Use Generics First if Possible — Many popular medications have already converted to generic status or will be doing so very soon. Prices for generic products are usually about 25% less than the brand during their first year on the market, and then may fall as low as 80% less thereafter.³ Unfortunately, when a drug goes generic, there is little or no marketing of the product and use may decrease. Many providers have been lead to believe that generic products are inferior to brand-name products. It is clear that this is not the case and the FDA carefully regulates quality and ensures equivalence before a generic drug can be substituted for the equivalent brand-name product. Most important is to use products that are available generically in place of other drugs in a class that are brand-only but have similar clinical effects. Table 2 provides examples of commonly prescribed brand name drugs, for which similar generic drugs can be used at a much lower price.

Carefully Evaluate New Drugs — Using newer, more expensive agents in place of older drugs is one of the largest factors contributing to higher drug prices. While some newer drugs may offer improvements to existing therapies, many do not. It is important to critically evaluate new drugs and make sure there is adequate evidence to support claimed advantages. Uwe Reinhardt, an economist from Princeton, discussed a serious deficiency in medical literature regarding the efficacy of newer products when compared with the progenitor products.⁴ Head-to-head comparative literature simply does not exist. Generally, we are using these newer agents because we believe them to be better, or because increased marketing suggests that they are better, but there is often very little evidence to support claims that are made or inferred. Frequently, drugs are released without much information about long-term use, or use outside of the carefully defined populations of clinical trials. Once released, problems can occur that may be serious enough to bring about a withdrawal from market. Recent examples of this phenomenon include Redux, Lotronex, Rezulin, Posicor, Seldane, Propulsid and Duract. Several excellent sources of information about new drugs include the Medical Letter, pharmacy and therapeutics committees and clinical pharmacists. The FDA website, www.fda.gov, posts transcripts of many advisory committee meetings that can provide extensive information about new drugs.

Avoid Unnecessary Use of Medications — This is particularly important with antibiotic use. Not only is unnecessary prescribing financially costly, but it is harmful in terms of limiting antibiotic effectiveness. Antibiotic-resistant

• **RISING COSTS** - continued from page 4**Table 1.** Less expensive options for commonly prescribed drugs

Prescribed Drug	Cost (\$)*	Alternative Drug	Cost (\$)*	Cost Savings (\$)
Prevacid 30 mg qd x 30 days	107	Protonix 40 mg qd x 30 days	81	26
Prilosec 40 mg qd x 30 days	157			76
Biaxin 500 mg bid x 10 days	71	Zithromax 250 mg qd (Z-pak dosing)	39	32
Levaquin 500 mg qd x 10 days	77	Tequin 400 mg qd x 10 days	67	10
Norco 10/325 1 tab qid x 30 days	92	hydrocodone/APAP 10/500 1 tab qid x 30 days	44	48
		hydrocodone/APAP 7.5/500 2 tabs qid x 30 days	43	49
OxyContin 40 mg bid x 30 days	223	MS Contin 30 mg tid x 30 days	151	72
Cozaar (losartan) 50 mg qd x 30 days	38	Micardis (telmisartan) 40 mg qd x 30 days	37	1
		Micardis (telmisartan) 80 mg ½ tab qd x 30 days	21	17
Actos 15 mg qd x 30 days	80	Metformin 500 mg bid	47	33
Avandia 4 mg qd x 30 days	70			23

* Costs of brand name products are reported as AWP - 13% + \$2.50.

This represents a common reimbursement equation. Costs of generic products are reported as MAC + \$2.50, again a common reimbursement method for generics.

Streptococcus pneumoniae is becoming an ambulatory care epidemic and is directly related to the overuse of antibiotics. Recent guidelines in the Annals of Internal Medicine suggest that most adult acute respiratory tract infections need not be treated with antibiotics.⁵ Studies indicate that the addition of antibiotics has relatively little effect on the duration and outcome of these types of infections. Additionally, mild to moderate cases of otitis media will often resolve on their own without the use of an antibiotic. There is no benefit to treating colds or the flu with antibiotics unless a secondary infection establishes itself. Many clinics have initiated a program in which physicians dispense or prescribe a "cold and flu" kit, containing acetaminophen for aches and fever, antihistamines and decongestants for nighttime and daytime symptom relief and written advice addressing expected symptom duration and non-pharmacologic methods for treating symptoms.

Dosing Strategies and Using Half-Tablets – Many drug products have a single price for different strengths, so the price is not proportional to the amount of active ingredient. Using half-tablets when appropriate can result in substantial savings. Cohen and Cohen reported in April 2000 that there was a potential savings in the U.S. of up to \$1.45 billion annually, just from splitting the newer psychotropic agents.⁶ There has been a lot of press regarding this issue lately, and while half-tab use should not be mandated, if the patient and the drug have been carefully selected, it can be a powerful method of cost-savings.

Selecting the Right Medications for Tablet Splitting – One of the most important aspects of this process is selection of the appropriate medication. It is critical to select medications for stable chronic conditions whose steady-state pharmacokinetics allow minor variations in total dose from day to day without affecting the response to the drug. Data suggest that a weight variance of 10-20% can occur in split tablets.^{7,8} Medications that are enteric-coated should not be split, nor should many extended- or controlled-release products. Medications that routinely break or crumble should also not be selected for tablet-splitting. Some non-scored tablets and tablets with asymmetric shapes can be split, but these should be evaluated carefully before initiating tablet splitting.

Generally, patients should not split a month's supply of tablets all at one time, as this can increase the amount of drug lost in crumbling. It is best to cut one tablet at a time, and then use the other half-tablet for the next dose.

Patients Need to be Carefully Selected, Too – In order for a tablet-splitting program to be successful, the patients need to be carefully

selected and educated regarding the process.⁹ Patients with physical disabilities such as visual impairments should not be expected to split tablets. Likewise, patients with arthritis, Parkinson's disease or other conditions that cause tremors or loss of dexterity should not split tablets. Patients with cognitive impairment or memory deficiency should only split tablets if they have a daily caregiver who is educated in the process and can assist with the task. Patients and caregivers who are resistant to the idea of using half-tablets should not be made to do so, as it is more important to ensure compliance and to maintain the correct dosages.

Table 2. Generic options for commonly prescribed drugs

Prescribed Drug	Cost/Year (\$)	Alternative Drug	Cost/Year (\$)	Cost Savings/Year (\$)
Pepcid 20 mg bid	1236	cimetidine 400 mg bid	108	1128
Axid 150 mg bid	1320			1212
Pepcid 20 mg bid	1236	ranitidine 150 mg bid	276	960
Axid 150 mg bid	1320			1219
Valtrex 500 mg bid	2208	acyclovir 400 mg bid	504	1704
Famvir 250 mg bid	2328	acyclovir 400 mg bid	504	1824
Relafen 500 mg bid	876	etodolac 400 mg bid	276	600
Daypro 600 mg ii caps qd	1080	naproxen 500 mg bid	144	936
Mobic 7.5 mg bid	1272	salsalate 1000 mg bid	336	936
Toprol XL 50 mg qd	228	atenolol 50 mg qd	60	168
Covera HS 240 mg qhs	600	verapamil (Calan SR) 240 mg qd	384	216
Accupril 20 mg bid	720	captopril 50 mg bid	120	50

Patient Education – When patients have been selected for making use of half-tablets, it is important that they understand the process and the correct doses. Commercially available tablet-cutters are available for splitting tablets.

Table 3. Half-tablet usage for common drug dosing

Prescribed Drug	Cost/Year (\$)	Preferred Drug	Cost/Year (\$)	Cost Savings \$/Year
Zestril (lisinopril) 20 mg qd	348	Zestril 40 mg ½ tab qd	264	84
Zestril 10 mg bid	636			372
Zoloft (sertraline) 50 mg qd	792	Zoloft 100 mg ½ tab qd	420	341
Celexa (citalopram) 20 mg qd	708	Celexa 40 mg ½ tab qd	384	324
Paxil (paroxetine) 20 mg qd	828	Paxil 40 mg ½ tab qd	456	372
Lipitor 20 mg bid	2076	Lipitor 80 mg ½ tab qd	576	1500
Micardis 20 mg qd	444	Micardis 40 mg ½ tab qd	252	192
Zomig 2.5 mg po prn (4 headaches treated with 2 doses per month)	1260	Zomig 5 mg ½ tab po prn (4 headaches treated with 2 doses per month)	732	528
Imitrex 50 mg po prn (4 headaches treated with 2 doses per month)	1368	Imitrex 100 mg ½ tab po prn (4 headaches treated with 2 doses per month)	696	672
Zocor 20 mg qd	1332	Zocor 40 mg ½ tab	684	648
Mavik (trandolapril) 2 mg qd	288	Mavik 4 mg ½ tab qd	156	132

CONCLUSIONS – The cost of health care continues to rise, and prescription drug costs remain a significant contributor to this increase. Fortunately, prescribers can help curb this increase by becoming better informed about drug prices. Clinicians can help contain prescription costs, while ensuring quality care by periodically reviewing patient's drug profiles, selecting generics when appropriate for care, avoiding the use of unnecessary medications and by carefully evaluating new drugs using evidence-based research before

• **RISING COSTS** - continued from page 5

including them in one's arsenal of commonly prescribed drugs. Finally, clinicians can help decrease drug costs by selecting once-daily drug regimens, or half-tablet doses when they are appropriate.

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More on COX-2 Inhibitors: CLASS and VIGOR Studies Prompt a New Debate - GI Safety versus Cardiac Risk

By: **Michele Koder, Pharm.D.**

The cyclooxygenase-2 inhibitors or COX-2s, celecoxib (Celebrex, Pharmacia/Pfizer) and rofecoxib (Vioxx, Merck), continue to be a controversial topic. On February 7th and 8th, 2001, Pharmacia/Pfizer and Merck aimed to demonstrate improved gastrointestinal (GI) safety over traditional NSAIDs to the FDA's Arthritis Advisory Committee. Upon submission of the original new drug applications (NDAs) in 1999, there was evidence of comparable efficacy and reduced incidence of endoscopic ulcers with COX-2s relative to the comparator NSAIDs studied (ibuprofen, diclofenac, and naproxen). Yet, the clinical significance of endoscopic ulcers has long been a matter of debate. Since the original NDA databases did not differentiate COX-2s from the comparator NSAIDs in terms of GI symptoms or PUBs (gastroduodenal Perforations, symptomatic Ulcers, or Bleeds), the standard NSAID GI warning template was included in the labeling for both products. Subsequently, the manufacturers conducted postmarketing studies, the Celecoxib Long-Term Arthritis Safety Study (CLASS) and the Vioxx Gastrointestinal Outcomes Research Study (VIGOR), in an attempt to resolve this issue. Based on results of these studies, the manufacturers submitted supplemental NDAs in which they petitioned the FDA to remove the NSAID GI Warning Template from their product labels. The Arthritis Advisory Committee's recent task was to review the CLASS and VIGOR studies and provide recommendations to the FDA regarding these petitions.

CLASS and VIGOR Highlights – CLASS and VIGOR were large, double-blind, randomized, comparator-controlled, company-sponsored studies designed to compare the incidence of clinically meaningful GI safety outcomes (eg, PUBs) of COX-2s to nonselective NSAIDs.^{1,2} A summary of each is available in Table 1.

CLASS represents 1441 and 1384 patient-years of exposure for celecoxib and NSAIDs respectively. Approximately 57% of patients completed 6 months of therapy. CLASS did not demonstrate a statistically significant advantage in terms of the primary endpoint (complicated PUBs) at any time for celecoxib compared to NSAIDs, although trends were evident in favor of celecoxib. Post-hoc analysis of upper gastrointestinal (UGI) complications in the non-aspirin cohort resulted in an annual incidence of UGI complications of 0.44 % (n = 5) in the celecoxib group versus 1.27 % (n = 14) in the NSAID group (RR = 0.35; p = 0.04). Aspirin use, which was permitted, increased the risk of UGI complications by over 4-fold in the celecoxib group (p = 0.01) but not in the NSAID group. No significant

differences were evident with respect to global safety and cardiac events, although there was a trend toward increased angina episodes and myocardial infarctions in the celecoxib group.

In VIGOR, the mean drug exposure was 8 months (range 0.5-13). About 29% of patients in each group discontinued their medication prior to study termination. Treatment with rofecoxib did result in significant reductions in both primary and secondary endpoints (PUBs and complicated PUBs respectively). The relative risk reduction was maintained in all important subgroups (eg, patients with a prior history of PUB, increased age). The number-needed-to-treat (NNT) to prevent 1 PUB was 62 and to prevent 1 complicated PUB was 191. Aspirin use was not permitted in the study. Furthermore, despite low absolute event rates (rofecoxib 1.7 % and naproxen 0.7 %), significantly more patients in the rofecoxib group experienced confirmed, cardiovascular thrombotic events, particularly myocardial infarctions, compared to naproxen. The RR for naproxen was 0.42. In a post-hoc analysis of patients in whom aspirin cardioprotection was "indicated" based on cardiovascular disease (CVD) risk factors and national guidelines, the RR for naproxen was 0.20. The corresponding NNT to result in a cardiovascular event was 156 for the entire patient population and 15 for patients with an indication for aspirin. It is expected that this NNT would be lower in the subset of patients at high risk for CVD events. Patients receiving rofecoxib also experienced more hypertension and congestive-heart-failure adverse events.

In each study, there was no separation between the time-to-UGI event curves until after 30-90 days. Therefore, there does not appear to be an advantage of COX-2s when used short-term. CLASS, VIGOR, and postmarketing data³ confirm the high risk of complicated ulcers in elderly patients (>65 years) and in patients with a prior history of ulcer disease or using steroids. Finally, the absolute event rates of UGI events in both studies were consistent with the range reported for the NSAID class in the GI warning template.

In summary, the risk reduction in UGI events did not translate into an overall safety benefit of rofecoxib or celecoxib over the comparator NSAIDs studied. Evaluation of routine safety parameters (deaths, serious adverse events, dropouts) showed no significant difference.

Table 1: CLASS and VIGOR Summary

	CLASS	VIGOR
Number Enrolled	8059	8016
Patients	OA and RA 69% Female Mean age 60 ~40% • 65; ~12% • 75	RA 80% Female Mean age 58 ~25% • 65; ~5% • 75
Randomization (n)	celecoxib 400 mg bid* (3987) ibuprofen 800 mg tid (1985) diclofenac 75 mg bid (1996)	rofecoxib 50 mg bid* (4047) naproxen 500 mg bid (4029)
Mean Exposure (Months)	4.2	8
Aspirin Use	>20%	No
UGI Complications, Annualized % (n) NNT for COX-2	RR = 0.53 (NS) 1• Outcome NNT=442	RR = 0.4 (p=.005) 2• Outcome NNT=191
Symptomatic Ulcers + UGI Complications, Annualized % (n) NNT for COX-2	RR = 0.59 (p = 0.02) 2• Outcome NNT=209	RR = 0.5 (p < 0.001) 1• Outcome NNT=62
MI % (n)	0.5 (19); 0.3 (14)† RR = 0.9 (NS)	0.4 (20); 0.1 (4) RR = 0.2 (p-NR)
NNT for rofecoxib CV event; CV event in ASA-indicated patient		NNT=156 NNT=15
Withdrawals due to Adverse Events	18.4 (732) 20.6 (822) RR = 0.89; (p < .01)	16.4 16.1 RR = 1.02; (NS)

OA = osteoarthritis; RA= rheumatoid arthritis; UGI= upper gastrointestinal, NR=not reported, NS=non-significant

* Higher than maximum recommended dose. The maximum recommended dose is 200 mg bid and 25 mg bid for celecoxib and rofecoxib respectively.

†Combined NSAIDs (ibuprofen plus diclofenac)

• **COX2 INHIBITORS** - continued from page 6

Arthritis Advisory Committee, Discussion and Recommendations – Present at the meeting were 4 rheumatologists, 1 gastroenterologist, 2 endocrinologists, 2 biostatisticians, 1 guest expert, 4 members of the FDA, 1 cardiologist, 1 consumer representative and manufacturer representatives. Committee members heard presentations from both Pharmacia/Pfizer and Merck, as well as gastrointestinal, medical/safety, cardiorenal, statistical and postmarketing safety reviews by expert members or consultants of FDA Advisory Committees. In their comprehensive review of material presented, members unanimously voted to retain the NSAID GI Warning Template for both celecoxib and rofecoxib on the basis of similar absolute event rates despite a relative advantage over NSAIDs.^{4,5} The panel concluded that neither study demonstrated a “clinically meaningful” overall safety advantage for COX-2s over NSAIDs or supported a superiority claim for either product. The committee acknowledged that there is a large continuum of adverse event rates within the nonselective NSAID class and that it is difficult to generalize data from both CLASS and VIGOR to the general population.

It is evident from both CLASS and VIGOR that concomitant aspirin complicates the benefit-risk ratio since aspirin appears to offset the GI safety advantage of COX-2s. The committee expressed concern over the fact that the age group most likely to receive COX-2s is also the age group with the highest cardiovascular mortality and which is most likely to be on low-dose aspirin for either primary or secondary prevention. The committee noted that it is difficult to make general conclusions regarding UGI and cardiovascular toxicity based on post-hoc analyses of aspirin and non-aspirin-using subgroups and non-prespecified endpoints. They recommended that additional studies be conducted to further evaluate the concomitant use of aspirin and COX-2s. Also recommended were nonspecific additions to the products' labeling warning of cardiovascular safety and concurrent aspirin use.

Pharmacia/Pfizer and Merck disputed the committee recommendations in further discussions with the FDA. Subsequent press releases issued from both manufacturers in mid-April stated that the FDA has issued letters that GI labeling changes have been deemed “approvable” contrary to the recommendation of the advisory committee.^{6,7} “Approvable” letters typically indicate the FDA's willingness to approve an application with the caveat that certain criteria be met or additional information be submitted. The letters do not contain the revised labeling. Although not required, the FDA usually follows advisory committee recommendations. If confirmed, these decisions mark a rare divergence on the part of the FDA.

Table 2: NSAID / COX-2 Cost Comparison⁸

Drug	Usual Dose	Cost per Month **	Cost per Year **
Salsalate*	1500 mg BID	\$ 30	\$360
Ibuprofen*	600-800 mg TID	\$ 7-10	\$84-120
Naproxen*	500 mg BID	\$ 10	\$120
Diclofenac*	75 mg BID	\$ 40	\$ 480
Celecoxib	200 mg QD	\$ 67	\$ 804
	100 mg BID	\$ 79	\$ 948
	200 mg BID	\$ 134	\$ 1608
Rofecoxib	12.5 mg QD	\$ 67	\$ 804
	25 mg QD	\$ 67	\$ 804
	50 mg QD	\$ 98	\$ 1176

* Cost of generic product.

**AWP-11% or HCFA MAC rounded to the nearest dollar

CONCLUSION – These trials underscore an important dilemma when assessing the overall benefit:risk ratio of the COX-2s versus nonselective NSAIDs. It is difficult to make large generalizations based on CLASS and VIGOR due to the relatively short duration of the studies, the limitation to a small sample of the NSAID class and the exclusion of patients on aspirin in VIGOR. In theory, as the risk for developing arthritides such as osteoarthritis and rheumatoid arthritis increase with age, so does the risk of CV disease. In patients predisposed to CVD, a GI safety advantage of COX-2s may be offset by a cardiovascular detriment; therefore, the decision to use COX-2s or nonselective NSAIDs is highly dependent on individual patient characteristics and risks.

Based on the results of CLASS and VIGOR, the patients most likely to benefit from COX-2s are patients with risk factors for PUBs (eg, age > 60 years, history of PUB or corticosteroid use) and who are not taking, or are

not candidates for aspirin cardioprotection. For patients at high risk for PUBs who require an NSAID and aspirin for cardioprotection, a nonselective NSAID plus a cytoprotective agent (eg, ibuprofen plus misoprostol or a proton pump inhibitor) would be preferred. For patients with low GI risk, salsalate, which exhibits a degree of COX-2 selectivity, remains a less costly alternative. Patients who fail 2 or more nonselective NSAIDs are also potential candidates for COX-2s. Short-term use of COX-2s is not recommended due to a lack of benefit over nonselective NSAIDs.

The comparative costs of COX-2s and NSAIDs remain an important factor in clinical decision-making. The COX-2s ranked among the top selling drugs in 2000.⁹ Celebrex ranked #6 on the list, earning over \$2 million, while Vioxx, with over \$1.5 million in sales, ranked #13. Table 2 provides a comparison of costs to OMAP.

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DUR Board Vacancies

The DUR Board is a federally mandated board of health care providers that review and comment on the Prospective and Retrospective Drug Use Review programs for fee-for-service Medicaid recipients, administered by the Office of Medical Assistance Programs (OMAP). Education efforts (including this newsletter) addressing inappropriate prescribing patterns are a responsibility of the Board. It is also responsible for reviewing OMAP drug use policies and making recommendations to the agency.

The Oregon DUR Board is recruiting for two physician positions and one pharmacist position for the twelve-member board, which meets quarterly. This is an opportunity to have a voice in Oregon Medicaid drug use policy. Qualified persons must have experience in prescribing or dispensing drugs to Medicaid recipients or expertise in drug use review or quality assurance. Please make this announcement known to others who may be interested.

Interested persons may inquire by phone (503) 494-1589, or submit a CV to Kathy L. Ketchum at:

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Portland Campus at OHSU
840 SW Gaines, MC 212
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We hope you found this issue of the Oregon Drug Use Review Board Newsletter useful as well as thought-provoking and interesting. We welcome your questions, concerns, comments or ideas regarding the newsletter. Address any correspondence to:

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Address Changes: Oregon Medicaid providers and pharmacies can provide OMAP with change of address information by fax at: (503) 945-6873 or by calling: 1-800-422-5047.

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Community Wall

The Divide Over Pill-Splitting

Experts disagree on whether this cost-saving tactic is a safe and effective practice

The cost of some medications -- many of them widely used -- can be reduced by as much as 50 percent when patients split one high-dose tablet in half to achieve the potency of the prescribed lower dose.

It's a way of getting the medication you need at a significant savings. But pill-splitting is also at the heart of the prescription drug debate. Some experts say while it makes sense mathematically -- cutting one high-dose tablet in half to yield the dosage of two lower-strength pills -- they question whether it actually bodes well biochemically: Are patients really getting one-half of the higher dose?

Even as questions abound on do-it-yourself pharmacy, a growing number of studies have begun to show that pill-splitting is a feasible way to treat a wide range of ills and, at the same time, dramatically lower costs.

"Sometimes, it is medically necessary, and it can be done," said Curtis Kellner, director of pharmacy at the University Hospital and Medical Center at Stony Brook.

Kellner, however, is not a fan of pill-splitting.

Some people have vision problems and can't split tablets, he said. Others have arthritis. "I can't imagine my own folks splitting tablets," Kellner said of his parents.

Cost was the only reason Kellner could find to justify splitting medications. He could see no sound medical reasons to endorse the practice.

But pill-splitting is catching on as more and more patients and insurers turn to it to beat back the rising cost of prescription drugs.

The idea behind pill-splitting stems from the way in which prescription drugs are made and priced. Many tablets are "scored," meaning they have



A scored pill inside an EZY Dose Deluxe Tablet Cutter; some drug manufacturers score pills to make them easier to split into roughly equal doses.

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Pill-Splitting: Is It Safe and Effective?

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a line running through the middle. When patients purchase the higher dose of their prescribed medication, cutting tablets along the score essentially yields two lower doses.

Tom Johnson, a pharmacist at Jones Drug Store in Northport, said pills are purposely scored by manufacturers. "This makes it easier for patients to take a lower dose," he said. "Midway through therapy, the doctor may decide the patient needs only a half dose. In that case, a patient can use a pill cutter to lower the dose." The score line through the tablets was added to help patients save money. However, pharmacists and physicians emphasize that patients should be trained in pill-splitting before they attempt it.

Some tablets should not be scored because they have extended-release properties built into their design. In fact, tablet function often dictates design, said pharmacist Vincent Terranova, also of Jones Drug Store. Having a drug remain active for 12 to 15 hours is vital in the treatment of several medical conditions.

While scoring does not interfere with the activity of dozens of types of medications, breaking pills that are not designed that way can destroy properties in the coating, resulting in too much or too little medication.

"Years ago, you might have gotten a prescription to take one tablet four times a day; now, you don't have to do that. You may take one capsule daily or two times a day," the result of extended-release properties in nonscored tablets.

"Every few hours, medication is released in a certain amount. If you break that tablet, you will interfere with the extended-release mechanisms," Terranova said.

Many -- but not all -- drugs that are scored can be cut in half. Patients can split pills, using a special blade that can be purchased at pharmacies for \$5 to \$10.

The practice becomes an economic strategy, some experts say, because the lower and higher strengths of any given medication usually cost about the same. For example, at drugstore.com, 30 10-milligram tablets of the antidepressant Paxil cost \$72.02. The same amount of tablets in the 20-milligram dose sells for \$76.80. With pill-splitting, patients can get twice as much medication for only a few dollars more.

Additionally, doctors have identified all manner of tablets that can be split: those that impede pain, those for high cholesterol, depression, hypertension, and male erectile dysfunction, to name a few.

Medications, like the antidepressant Celexa, generically known as citalopram hydrobromide, are so deeply scored on both sides, that a 40-milligram tablet can be easily snapped in half by hand to yield the lower, 20-milligram dose, doctors say.

Medical experts who favor pill-splitting say people have been doing it for years. "This is a practice that has been present at a low level for a very long time," said Dr. Randall Stafford, a professor of medicine at Stanford University Medical Center in Palo Alto, Calif.

Stafford, who led a major study on the feasibility of pill-splitting, said the practice renders high-cost medications imminently affordable. And he believes it is an idea worth considering by anyone lacking prescription-drug insurance coverage. He and his team identified a range of medications that could be safely split to yield a cost savings.

"The potential cost savings with pill-splitting are not trivial," Stafford said, "and are in the range of \$25 a month for most of the drugs we identified." In his investigation, Stafford identified 11 commonly used medications that could be safely split.

Increasingly, patient advocacy groups, insurers and health maintenance organizations have begun to embrace the practice. The Veterans Administration permits pill-splitting for its patients, as does Kaiser Permanente, the largest health maintenance organization in the country.

The Illinois Medicaid program now requires patients who receive prescriptions for the 50-milligram dosage of the antidepressant Zoloft to buy the 100-milligram tablets instead, and split them in half. This instantly doubles the number of tablets patients have available at about the same cost of the 50-milligram pills. Illinois Medicaid reimburses patients only for the higher-dose tablets.

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However, the American Medical Association, the American Pharmaceutical Association and the American Society of Consultant Pharmacists have openly opposed mandatory pill-splitting by insurers. They cite potential underdoses or overdoses of drugs as a consequence.

A recent report in the *Journal of the American Pharmaceutical Association* on splitting nearly a dozen commonly used drugs, found the practice rests on the cutter's ability to accurately halve the medication. Most people tested, the study found, could neither accurately nor safely split the drugs.

John Broder, spokesman for Winthrop University Medical Center in Mineola, said neither pharmacists nor doctors there recommend the practice. However, pill-splitting is endorsed in instances when hospital physicians prescribe a dosage that is not available commercially.

"The emphasis here is that individuals should not take it upon themselves to split a dosage to make a prescription last longer," Broder said.

But patients, some doctors say, are expressly asking to be informed about the benefits and drawbacks of pill-splitting.

"The issue of pill-splitting first came to my attention," Stafford continued, "because patients came to me requesting it. By and large, these were patients who did not have insurance coverage for their medications."

Kellner, however, is more concerned about what patients obtain after they split their pills.

"There are other issues people have to be concerned with," Kellner said. Some drugs are film-coated, he said, and must remain intact to be properly absorbed. Still others, he said, are oddly shaped and cannot be split to yield two effective doses.

Viagra, Pfizer's small blue pill for male erectile dysfunction, is so small that a special splitter has been developed to permit patients to cut the dose in half.

Nevertheless, Kellner still sees a problem with splitting small tablets, especially those developed to treat serious maladies. "Even though digoxin is scored," he said of the drug also known as digitalis and prescribed for heart failure, "it is too tiny to safely split. So if you're going to endorse tablet-splitting, you'll also have to set rules about which tablets can and cannot be cut. With digoxin you'd wind up with two little crumbs."

He also emphasized that tablets do not contain the exact amount of medication in the two halves, a fact already well known by health officials at the Food and Drug Administration. People who need an exact dose of their medication could fall far short because of the way a tablet is manufactured, Kellner said.

Rather than patients splitting their pills at home, Kellner said he'd prefer to see an end to what he calls "predatory pricing" by pharmaceutical companies.

"Drugs are becoming more and more a significant cost of health care, and it is a tremendous problem," Kellner added. "Drug budgets of hospitals have more than doubled in the last couple of years because of the cost of pharmaceuticals."

But researchers such as Stafford say patients need relief from the costs. "We're not advocating this as a global solution," Stafford said of drug-splitting. "It needs to be conducted within the context of a doctor-patient communication." He highly recommends that anyone considering the practice use only a special pill-cutting blade and to be trained by a pharmacist in its use.

Stafford acknowledges that many groups of patients are not even candidates for the practice: those with poor eyesight, severe arthritis affecting their hands, dementia or psychosis.

But Stafford's analysis also revealed the dramatic sums that can be saved with drug-splitting. He and his team assessed the costs of a Massachusetts-based health plan before wide-scale pill-splitting and what could be saved if it were endorsed.

Only a few doctors in the plan encouraged the practice prior to the study and did so infrequently. The result was an average cost savings of \$6,200 for the insurer. If, instead, the plan pushed pill-splitting for the 11 medications Stafford identified as safe to cut, the plan would save \$259,500 a year.

The practice can prove equally dramatic for individuals. Stafford found, for instance, that patients prescribed the 10-milligram tablets of Zestril for congestive heart failure can realize a significant savings by buying the 20-milligram strength and splitting the pills.

For the 10-milligram strength, the cost is about \$340 a year Stafford estimated. By cutting the 20-milligram tablet in half, the cost would be only \$180, Stafford said.

Warning: Do not make any changes in your medications or the way you take your medications without first talking it over with your doctor.

Source: *Newsday* - Nov. 19, 2002

RELATED LINKS AND INFO

[A Look At Pill Splitting](#)

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For more information about pill splitting, go to the [American Society of Consultant Pharmacists Web site](#).

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The Potential of Pill Splitting to Achieve Cost Savings

Randall S. Stafford, MD, PhD; and David C. Radley, BA

Objectives: To present a methodology for identifying specific medications for which pill splitting is clinically appropriate and cost saving, to present data from a commercial managed care population on current pill-splitting practices, and to estimate additional cost savings from extended use of this strategy.

Study Design: Retrospective pharmacy claims analysis.

Methods: Pharmacy claims data from a commercial managed care health plan covering 19,000 lives and national drug data were used to compile a list of frequently prescribed medications. Excluding medications in which packaging, formulation, and potential adverse pharmacologic outcomes prohibited splitting, we performed a cost analysis of medications amenable to splitting.

Results: Eleven medications amenable to pill splitting were identified based on potential cost savings and clinical appropriateness: clonazepam, doxazosin, atorvastatin, pravastatin, citalopram, sertraline, paroxetine, lisinopril, nefazadone, olanzapine, and sildenafil. For these medications, pill splitting is currently infrequent, accounting for annual savings of \$6200 (or \$0.03 per member per month), just 2% of the potential \$259,500 (or \$1.14 per member per month) that more comprehensive pill-splitting practices could save annually.

Conclusions: Pill splitting can be a cost-saving practice when implemented judiciously using drug- and patient-specific criteria aimed at clinical safety, although this strategy is used infrequently.

(*Am J Manag Care* 2002;8:706-712)

In recent years, the cost of prescription drugs has accelerated drastically. Patients, insurers, and provider networks continue to bear the burden of prescription drug costs, which have increased nearly 60% since 1991 and tripled since 1980.¹

To alleviate rising prescription drug costs, physicians and providers have used various cost-saving strategies, including the use of generic medications, selection of more cost-effective medications, tiered systems of drug copayments, and formulary restrictions.

One cost-saving strategy that may not have yet reached its potential is pill splitting. Many prescription drugs are available at increased dosages for the same or similar costs as smaller dosages. By prescribing half as many higher strength pills and splitting them to achieve the desired dosage, patients and physician systems can save as much as 50% on the cost of selected medications. As a cost-saving approach, pill splitting has great potential. For example, a patient being treated with 10 mg lisinopril (Zestril; AstraZeneca Pharmaceuticals, Wilmington, DE) will have annual medication costs of \$340. By prescribing half the number of 20-mg tablets to be split, medication costs will drop to \$180 annually, savings of \$160 (47%).² Similarly, a recent study focusing on splitting psychotropic medications suggests the potential for annual national savings of \$1.4 billion.³

Pill splitting is a well-established medical practice,⁴ not uncommon in prescribing pediatric⁵ or geriatric dosages.⁶ However, fears of inaccurate dosing, noncompliance, and physical inability to split tablets have discouraged physicians and patients from adopting this practice. Opponents of pill splitting have cited unpredictable effects on the stability of the drug, loss of drug due to powdering, creation of uneven doses, lack of physical strength and dexterity, poor eyesight, reduced cognitive ability, and

From the Institute for Health Policy, Massachusetts General Hospital, Harvard Medical School, Boston, MA (RSS and DCR); the Stanford Center for Research in Disease Prevention, Stanford University, Palo Alto, CA (RSS); and the Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven CT (DCR).

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lack of instruction as arguments against pill splitting.⁴ However, prior studies suggest that most patients are able to accurately split pills with minimal loss of tablet content.^{4,7} With some notable exceptions, the chemical stability of most tablet formulations is not substantially altered by pill splitting.⁵ Concerns also have been expressed over patient adherence. There is a fear that prescribing higher dosages that require tablets to be halved will lower adherence: patients may not be willing to take the time to split a pill before taking it or may be unable to split a pill. Objectively, however, 1 study found that splitting tablets had no effect on adherence.⁸ It was further suggested that tablet splitting might increase adherence by reducing the cost barrier faced by some patients.⁸

Pill splitting is safer and easier when drug- and patient-specific criteria have been met. Medications should not be considered when packaging and pricing structure do not make splitting cost effective or even possible. Medications should not be split if splitting could result in adverse pharmacologic outcomes. Such medications include those with enteric coatings, extended-release formulations, a narrow therapeutic window, or a short half-life-to-dosing ratio. The use of pill-splitting devices can make splitting tablets easier for patients and often yields more accurate doses,⁹ and some physical properties of medications such as scoring, shape, and size affect the ease and accuracy of splitting.⁷

Patients should be instructed by pharmacists how to accurately split tablets manually or how to use a pill-splitting device. In most cases, patients should be comfortable with splitting their own medication, and they should be free from physical impairments, including poor eyesight, loss of a limb, tremors, debilitating arthritis, or any other condition that might hinder accurate pill splitting. Pill splitting by pharmacists may still be a viable option for impaired patients in selected states.⁴ Although consideration of these many factors suggests that pill splitting can be undertaken without compromising patient safety, explicit evaluation of this question has not been undertaken.

Pill splitting also has the advantages of making newer and expensive medications available to more people who might not otherwise be able to afford them, allowing physicians to individualize a patient's dosage when the medication is not available in the desired dosage, and offering cost savings without risking a withholding of needed services. Pill splitting for pediatric patients may have specific advantages regarding dosage, but may also require special caution.

Though a recent study suggests that pill splitting may be frequent in long-term care facilities,⁶ little is known about actual patterns of tablet splitting, particularly in ambulatory settings. This report describes a methodology for identifying medications amenable to pill splitting based on specific criteria, and uses pharmacy claims data to gauge current pill-splitting practices and the potential for additional cost savings.

METHODS

We investigated pill splitting within a commercial managed care population of 19,000 covered lives served by primary care physicians affiliated with the Massachusetts General Hospital (MGH). This population consisted of working-age beneficiaries receiving employer-based health insurance in the Boston metropolitan area.

We sought to identify specific medications for which pill splitting would be appropriate and cost saving in 2:1 splitting ratios; to determine current patterns of pill splitting among MGH physicians, to estimate the potential cost savings that would result from pill splitting; and to recommend guidelines for safe pill-splitting prescribing practices.

Pharmacy claims data from January 1, 2000, through August 30, 2000, were available for managed care members with MGH primary care providers. We compiled a list of the 265 most frequently prescribed proprietary and generic medications, both nationally² and within the MGH population. To determine medications amenable to splitting, we evaluated each medication using cost- and pharmacologic-specific criteria. Included were cost savings per dosage increase, based on the average wholesale price and actual costs to the health plan, pharmacokinetic interactions and therapeutic window, packaging, and formulation. Physical properties such as scoring and tablet size also were considered, although they were not necessarily determining factors for inclusion in this study.

Preliminary review of the 265 most frequently prescribed medications allowed us to eliminate 125 medications because pill splitting was not feasible. Among the most common reasons were that medications were available in only one dosage, that the medication was administered non-orally, that a capsule or other nonsplittable form was used, and that the tablets were prepackaged. Commonly prescribed medications available in a single dose

included fexofenadine (Allegra; Aventis Pharmaceuticals, Parsippany, NJ), oxaprozin (Daypro; G. D. Searle & Co., Chicago, IL), raloxifene (Evista; Eli Lilly and Company, Indianapolis, IN), and tramadol (Ultram; Ortho-McNeil Pharmaceutical, Raritan, NJ). Common nonoral medications included corticosteroid and β -agonist inhalers. Capsule formulations among frequently prescribed drugs include terazosin (Hytrin; Abbott Laboratories, Inc, North Chicago, IL), fluvastatin (Lescol; Novartis Pharmaceuticals Corporation, East Hanover, NJ), valsartan (Diovan; Novartis Pharmaceuticals Corporation, East Hanover, NJ), fluoxetine (Prozac; Eli Lilly and Company, Indianapolis, IN), and omeprazole (Prilosec; AstraZeneca Pharmaceuticals, Wilmington, DE). Oral contraceptives are the most common examples of prepackaged medications.

The remaining 140 medications were evaluated based on potential cost savings on a per-dosage basis. For continued consideration, a medication was required to have cost savings through splitting that exceeded 25% and/or \$0.40 per dosage (\$0.20 for generic medications) based on average wholesale price.² Of these 140 medications, 61 were eliminated because splitting offered no or minimal cost savings. Examples of commonly used medications that were eliminated because of the lack of per-dosage cost savings through pill splitting included buspirone (BuSpar; Bristol-Myers Squibb Company, Princeton, NJ), metformin (Glucophage; Bristol-Myers Squibb Company, Princeton, NJ), and famotidine (Pepcid; Johnson & Johnson/Merck, Fort Washington, PA).

Using the 1999 and 2001 *American Hospital Formulary Service Drug Information* indices,¹⁰ the 79 remaining medications were evaluated for potential adverse pharmacologic effects. Each medication was screened based on toxicity, rate of absorption, elimination half-life, and therapeutic window. Nine medications with a potential for adverse consequences from splitting were excluded based on manufacturer warning against pill breakage (eg, nitroglycerin [Nitrostat; Parke-Davis, Morris Plains, NJ]), nonproportional combination medications (amoxicillin-clavulanic acid [Augmentin; SmithKline Beecham, Philadelphia, PA]), narrow therapeutic window (eg, warfarin), or rapid half-life-to-dosing ratio (eg, tolterodine [Detrol; Pharmacia & Upjohn, Peapack, NJ]). The latter criteria refers to medications with elimination half-lives short enough relative to the dosing frequency to raise potential concerns about fluctuations in serum concentrations should splitting be inaccurate. Once-daily sertraline, with a half-life of 25 to 26 hours,¹⁰ is an

example of a medication with a substantial pharmacokinetic buffer against inaccurate pill splitting. Olanzapine was included because splitting is feasible as long as the split tablet is used within a week of splitting.

Twenty-two additional medications with extended-release formulations were excluded, as altering these medications' physical properties by splitting could negatively impact their pharmacokinetics. Examples of extended-release formulations included felodipine (Plendil; AstraZeneca Pharmaceuticals, Wilmington, DE), extended-release bupropion (Wellbutrin SR; Glaxo Wellcome, Inc, Research Triangle Park, NC), extended-release nifedipine (Procardia XL; Pfizer Inc, New York, NY; Adalat CG; Bayer Corporation, West Haven, CT), and isosorbide mononitrate (Imdur; Key Pharmaceuticals, Inc, Kenilworth, NJ).

A detailed cost analysis of the 48 remaining medications using data from the available pharmacy claims records allowed us to determine actual cost, current rates of pill splitting among MGH physicians, and potential savings from extended use of this strategy. Eliminating those medications with minimal usage in the MGH population, we identified 11 recommended medications for which pill splitting is clinically appropriate and cost saving. Enalapril (Vasotec; Merck & Co. West Point, PA), nefazadone (Serzone; Bristol-Myers Squibb Company, Princeton, NJ), mirtazapine (Remeron; Organon, Inc, West Orange, NJ), zafirlukast (Accolate; AstraZeneca Pharmaceuticals, Wilmington, DE), and clarithromycin (Biaxin; Merck & Co. West Point, PA) were examples of medications that could have been associated with cost savings if they were used more frequently in the MGH system.

To calculate current rates of pill splitting for these medications, we used the following methods: for each daily dose of each medication, we calculated the proportion of prescriptions for which 2-to-1 splitting was implied by the number of pills provided and the days of therapy supplied by the prescription. For example, for all patients prescribed lisinopril 10 mg per day, we compared the number achieving this dose via 10-mg tablets (30 tablets provided for 30 days) with the number achieving this dose via 20-mg tablets split 2-to-1 (15 tablets provided for 30 days). For each medication, we reported the aggregate rate of pill splitting across all possible 2-to-1 splitting possibilities. During our investigation, no organizational efforts were in place to promote pill splitting.

Our cost analysis was based on usage volume and the actual cost of select medications in a commercial HMO population. Our unit of analysis was the prescribed daily dose (mg/day) for each of the selected medications, whereas our outcome measures were the cost savings realized from halving higher-strength tablets to achieve the desired dosage. To estimate current costs and potential savings, we extracted the total number of days of therapy prescribed for each medication at each dosage for all

patients as well as the total number of days of therapy for each medication if higher-strength pills were split to achieve the desired dosage. We annualized our 8 months of data to represent expected utilization and costs for a full year. An annualized cost analysis indicated those medications for which sizable current or future cost savings could be expected from pill splitting.

Observed and potential cost savings were calculated using the following equations:

Table. Potential Cost Savings from Pill Splitting in a Commercial HMO Health Plan

Drug and Daily Dose (mg)		Cost in Health Plan Contract		Annual No. of Prescriptions	Observed Occurrences		Potential Annual Savings (\$)
		Per Pill (\$)	If Higher-Strength Pill Is Split (\$)		No. of Prescriptions From Splitting	Observed Annual Savings (\$)	
Clonazepam	0.5	0.40	0.24	380	-	0	1456
	1	0.47	0.26	79	-	0	510
Doxazosin (Cardura)	1	0.97	0.48	58	-	0	1207
	2	0.95	0.54	105	11	224	2320
	4	1.00	0.52	76	-	0	146
Citalopram (Celexa)	20	1.90	1.02	890	66	2409	25,758
Atorvastatin (Lipitor)	10	1.77	1.33	2184	3	120	44,746
	20	2.68	1.54	1121	-	0	62,465
Paroxetine (Paxil)	10	2.19	1.15	281	17	712	11,176
	20	2.19	1.21	468	-	0	15,202
Pravastatin (Pravachol)	10	2.03	1.09	88	-	0	4056
	20	2.17	1.74	481	-	0	11,209
Nefazodone (Serzone)	50	1.16	0.60	12	-	0	242
	100	1.19	0.60	33	-	0	565
Sildenafil (Viagra)	25	8.54	4.27	37	-	0	610
	50	8.52	4.27	513	-	0	8461
Lisinopril (Zestril)	2.5	0.55	0.45	85	20	123	415
	5	0.85	0.55	566	9	99	8265
	10	0.88	0.47	1214	-	0	23,754
	20	0.93	0.67	716	-	0	9708
Sertraline (Zoloft)	25	2.11	1.15	87	12	526	2656
	50	2.12	1.14	616	75	1669	20,535
Olanzapine (Zyprexa)	2.5	4.26	2.53	38	3	263	2302
	5	5.09	3.85	52	2	57	1752
Total cost savings						\$6202	\$259,516

Daily dosages reported here can be achieved as a whole tablet or from splitting a higher strength tablet in half. The highest reported daily dosage for each drug can be achieved from splitting a higher strength tablet not shown in the table.

Observed annual savings = (savings per day of therapy) \times (# of observed annual days of therapy achieved from pill splitting)

Potential annual savings = (savings per day of therapy) \times (total annual days of therapy)

RESULTS

Top Drugs for Splitting

We identified 11 medications for which pill splitting was clinically appropriate and could result in significant cost savings (Table). Of these medications, many are used for treatment of psychiatric disorders: clonazepam, citalopram (Celexa; Forest Pharmaceuticals, Inc, St. Louis, MO), paroxetine (Paxil; SmithKline Beecham, Philadelphia, PA), nefazadone, sertraline (Zoloft; Pfizer, Inc, New York, NY), and olanzapine (Zyprexa; Eli Lilly and Company, Indianapolis, IN). Also common were medications for lipid lowering: atorvastatin (Lipitor; Pfizer, Inc, New York, NY) and pravastatin (Pravachol; Bristol-Meyers Squibb Company, Princeton, NJ); and for hypertension: doxazosin (Cardura; Pfizer, Inc, New York, NY) and lisinopril. In addition, sildenafil (Viagra; Pfizer, Inc, New York, NY), a drug for erectile dysfunction, was included.

Of the 11 medications, 7 (70%) are scored: clonazepam, doxazosin, citalopram, paroxetine, nefazadone, lisinopril, and sertraline. The potential average cost savings from splitting was 36%. Cost savings ranged from 18% for lisinopril (2.5 mg dose) to 50% for doxazosin (1 mg), nefazadone (100 mg), and sildenafil (25 and 50 mg). Seventy-five percent (18 of 24) of the possible prescribed daily dosages for these medications could yield cost savings of at least 40% per pill.

Pill Splitting Is Currently Infrequent

Although pill splitting was used for a sizable number of HMO members, this practice was relatively infrequent. Splitting was most frequent for sertraline at a dose of 50 mg/day, for which 75 (12%) prescriptions were made from 100-mg tablets to be taken one half per day, compared with 616 (88%) receiving one 50-mg tablet once per day. Other medications for which splitting occurred were citalopram (8%), doxazosin (4%), and paroxetine (2%). Pill splitting was either negligible or not observed for the other selected medications.

Current and Potential Cost Savings

Among the selected 11 medications, we calculated that current pill-splitting practices saved \$6200

on an annualized basis, an equivalent of only \$0.03 per member per month. The largest contributor was citalopram (\$2400). Current cost savings, however, represent only 2.4% of the potential savings that could result from pill splitting among these 11 medications. Full use of tablet splitting for these drugs would generate \$259,500 in savings annually (or \$1.14 per member per month). The largest potential contributors to cost savings were atorvastatin (\$107,200), lisinopril (\$42,100), paroxetine (\$26,400), citalopram (\$25,700), sertraline (\$23,200), and pravastatin (\$15,300). Because not all patients should be considered for pill splitting, achievable savings would be less than these projections, although this report does offer a useful gauge of cost savings using this strategy.

DISCUSSION

Based on specific criteria focused on safety and frequency, we have identified 11 medications in which extended use of pill splitting could be cost saving for a commercial HMO plan. Of these medications, a preponderance were used to treat psychiatric disorders, hypertension, and hyperlipidemia. The selected medications shared relatively wide therapeutic windows, long half-life-to-dosing ratios, and substantial potential for cost savings. Pill splitting is currently infrequent among MGH physicians, accounting for only \$6200 in savings annually, just 2.4% of the potential \$259,500 that could be saved from extended use of this cost-reduction strategy for the selected medications. This represents overall savings of 36% off the costs of these selected medications.

A recent lawsuit alleging that a mandatory pill-splitting program adopted by one of the nation's largest health maintenance organizations jeopardized patient safety¹¹ highlights an important point about appropriate pill splitting: although the practice can save money, pill splitting should be considered only in the context of specific patient-physician assessment and discussion. Review of these legal issues suggests that physicians can reduce the liability risks associated with pill splitting by judiciously limiting pill splitting to those medications and patients for whom it is medically appropriate and by engaging in a candid discussion of the requirements, costs, and benefits of a pill-splitting regimen.

Pill splitting can be expected to be relatively safe when drug- and patient-specific criteria have been met. In addition to appropriate dialog between the

physician and the patient, the following medication characteristics should be considered in selecting medications for splitting:

- Wide therapeutic windows ensure a buffer against potential fluctuations in dosing that could occur because of inaccurate tablet splitting. This includes medications with a relatively large ratio of drug concentrations producing significant undesired effects to those producing desired effects.
- Fluctuations from misdosing also can be minimized by medications that have a long half-life relative to the frequency of dosing because steady-state drug levels are less sensitive to potential variation in individual doses.
- Drugs that have enteric coatings or that are formulated as extended release should not be split.
- Drugs that are prepackaged, such as oral contraceptives, should not be split.
- Medications that do not have a pricing structure that makes splitting cost effective should not be considered.
- Physical properties of medications affect the ease and accuracy of splitting. For example, tablets that are deeply scored or scored on both sides are easier to split than unscored tablets.⁷

Our list of medications incorporated these characteristics, as well as several others that were specific to our setting, including frequency of prescribing and pricing considerations. Whereas other systems may derive somewhat different lists of medications, the foundation for these decisions should always begin with drug characteristics.

Patient-specific characteristics are also vital to consider in tablet splitting. Patients should be willing and able to be instructed by pharmacists on how to accurately split tablets or in the use of a pill-splitting device and they should be comfortable with splitting their own medication. Additionally, patients should have no physical or cognitive impairments that could impede accurate pill splitting or reliable dosing once pills are split. While some states prohibit pharmacists from splitting tablets,⁴ pill splitting may still be a viable option for some impaired patients in selected states. For example, regulations controlling pharmacists do not include such a prohibition in Massachusetts, California, Oregon, and New York, among other states. Even where legal, however, lack of reimbursement to pharmacies for pill splitting may constrain the willingness of pharmacists to perform splitting.

The beneficiary of the cost savings generated by tablet splitting will vary depending on the system of

reimbursement. Self-pay patients or patients with capped pharmacy benefits will reduce their out-of-pocket expenses by splitting their pills. In other instances, physician systems or health insurance plans will realize the cost savings, as was the case with the population that we analyzed. For patients who would not otherwise benefit, it would be ideal if they could be offered an incentive to use split dosages (eg, a reduction in their copayment).

Out of convenience, we have used data from a commercial health plan, although data from other types of plans could augment our analysis. For example, information on a Medicare population would be appropriate given that elderly patients have greater medication use and experience greater out-of-pocket costs that could be diminished through pill splitting.

Limitations

Although we lack the information needed to estimate precisely the proportion of patients who are unwilling or unable to split pills, this proportion is likely to be smaller within an employed population compared with other populations. In our population, we estimated that approximately 10% to 30% of patients would be unable or unwilling to make use of prescriptions that require pill splitting. Our results, from a large academic medical center and its physicians, may not reflect current practices and potential cost savings in other practice settings. We focused only on medications that were preferred in the MGH managed care plan. This tactic excluded several drugs for which significant savings could be realized in other settings (ie, lisinopril as Prinivil was included, but not Zestril). We focused only on 2-to-1 splitting ratios, although savings may be significant with other dosing ratios (eg, prescribing 75 mg sertraline from splitting three 50-mg tablets over 2 days rather than three 25-mg tablets in one day).

We recognize that the potential cost savings as reported here might not be fully achievable, as pill splitting will not be appropriate for every patient. A number of factors may cause actual savings to fall below those potentially achievable, including a patient's unwillingness to accept split-dosing prescriptions, patient inability to split pills (either through self-splitting or through a pharmacist), and lack of familiarity by prescribers. Although we lack information needed to estimate the proportion of patients that fall into these categories, this proportion is likely smaller within an employed population compared with other populations.

Although many factors suggest that more widespread pill-splitting practices could be adopted without compromising patient safety, it was beyond the scope of this study to evaluate the safety of pill splitting in our population either currently or for our projections of increased splitting. A long-term consideration may be that consistent and widespread adoption of tablet splitting might result in pharmaceutical pricing strategies that eventually eliminate the advantages of splitting. More likely, however, is that some segments of the market for pharmaceuticals (eg, managed care or self-pay) may adopt pill splitting more than others.

Implications

Our analysis has indicated that significant cost savings are possible through tablet splitting for a set of medications selected using explicit criteria. We recommend that physicians talk with patients, review their medications, work with them to assess whether pill splitting is a viable option, and use this strategy when it can be carried out safely. The cost savings from this underused practice are significant and, if implemented judiciously, this strategy presents an opportunity to reduce healthcare costs without compromising quality.

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